11/19/04

10/621,520

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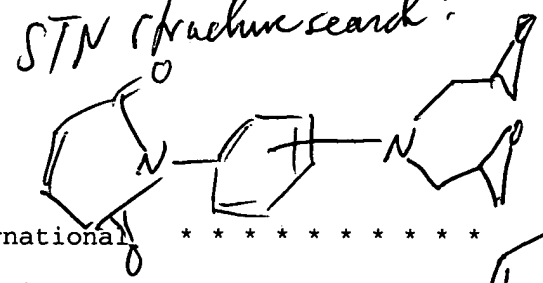
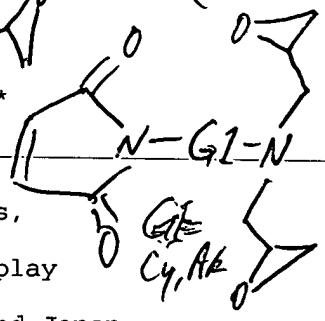
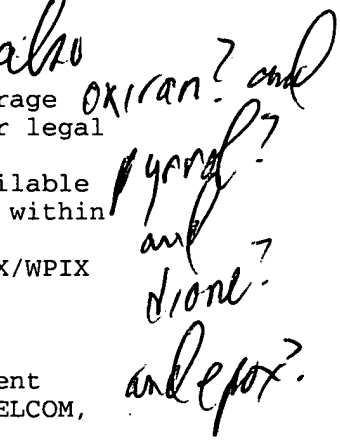
STN structure search:



and



also oxiran? and



yeast? and dione? and epox?

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
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NEWS	12	SEP 27	STANDARDS will no longer be available on STN
NEWS	13	SEP 27	SWETSCAN will no longer be available on STN
NEWS	14	OCT 28	KOREAPAT now available on STN
NEWS	15	NOV 18	Current-awareness alerts, saved answer sets, and current search transcripts to be affected by CERAB, COMPUAB, ELCOM, and SOLIDSTATE reloads

NEWS EXPRESS	OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
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NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:21:28 ON 19 NOV 2004

=> fil reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION

FULL ESTIMATED COST 0.21 0.21

FILE 'REGISTRY' ENTERED AT 11:21:36 ON 19 NOV 2004
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 17 NOV 2004 HIGHEST RN 783276-57-3
DICTIONARY FILE UPDATES: 17 NOV 2004 HIGHEST RN 783276-57-3

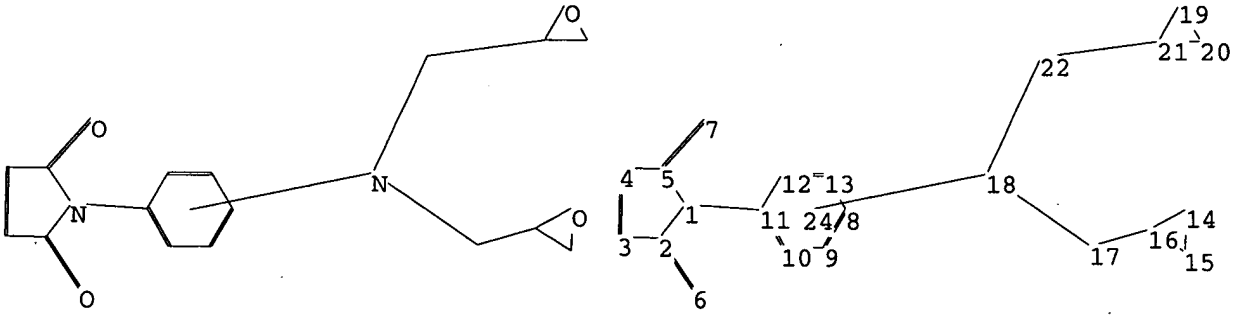
TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\MALEIMIDEEPOXIDE6.str



chain nodes :
6 7 17 18 22
ring nodes :
1 2 3 4 5 8 9 10 11 12 13 14 15 16 19 20 21
chain bonds :
1-11 2-6 5-7 16-17 17-18 18-22 21-22
ring bonds :
1-2 1-5 2-3 3-4 4-5 8-9 8-13 9-10 10-11 11-12 12-13 14-15 14-16 15-16 19-20 19-21 20-21
exact/norm bonds :
1-2 1-5 1-11 2-6 5-7 14-15 14-16 15-16 17-18 18-22 19-20 19-21 20-21
exact bonds :
2-3 3-4 4-5 16-17 21-22
normalized bonds :
8-9 8-13 9-10 10-11 11-12 12-13
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:CLASS 18:CLASS 19:Atom
20:Atom 21:Atom 22:CLASS 24:CLASS

L1 STRUCTURE UPLOADED

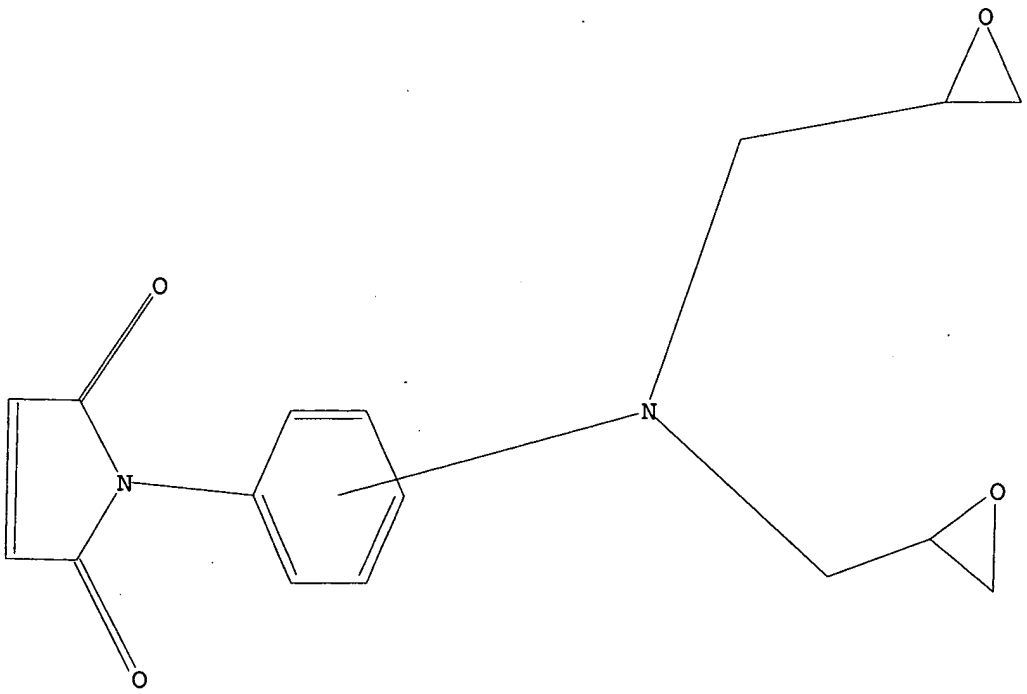
=> s L1
SAMPLE SEARCH INITIATED 11:21:56 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 39 TO ITERATE

100.0% PROCESSED 39 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 406 TO 1154
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> d L1
L1 HAS NO ANSWERS
L1 STR



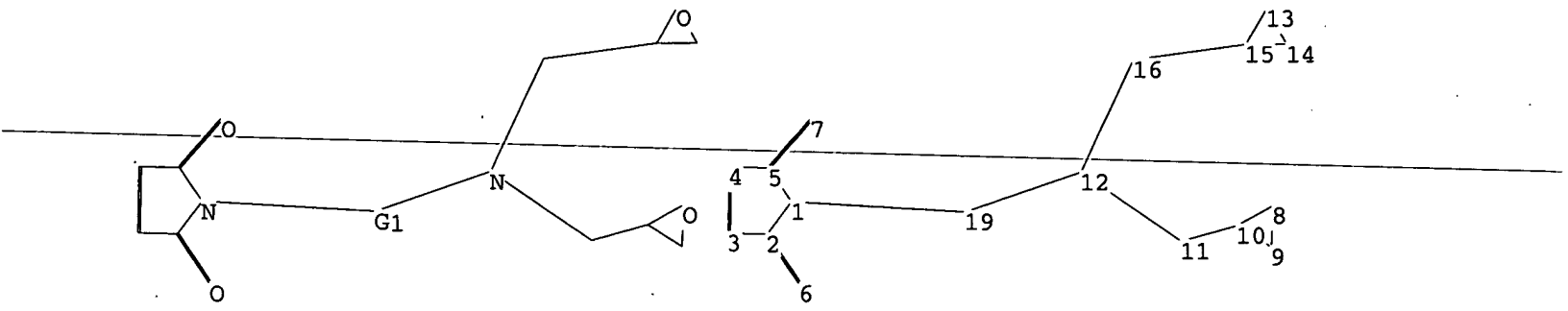
Structure attributes must be viewed using STN Express query preparation.

=> s L1 full
FULL SEARCH INITIATED 11:22:09 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 948 TO ITERATE

100.0% PROCESSED 948 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=>
Uploading C:\Program Files\Stnexp\Queries\maleimideepoxide7.str



chain nodes :
6 7 11 12 16 19
ring nodes :
1 2 3 4 5 8 9 10 13 14 15
chain bonds :
1-19 2-6 5-7 10-11 11-12 12-16 12-19 15-16
ring bonds :
1-2 1-5 2-3 3-4 4-5 8-9 8-10 9-10 13-14 13-15 14-15
exact/norm bonds :
1-2 1-5 1-19 2-6 5-7 8-9 8-10 9-10 11-12 12-16 12-19 13-14 13-15 14-15

exact bonds :
2-3 3-4 4-5 10-11 15-16
isolated ring systems :
containing 1 :

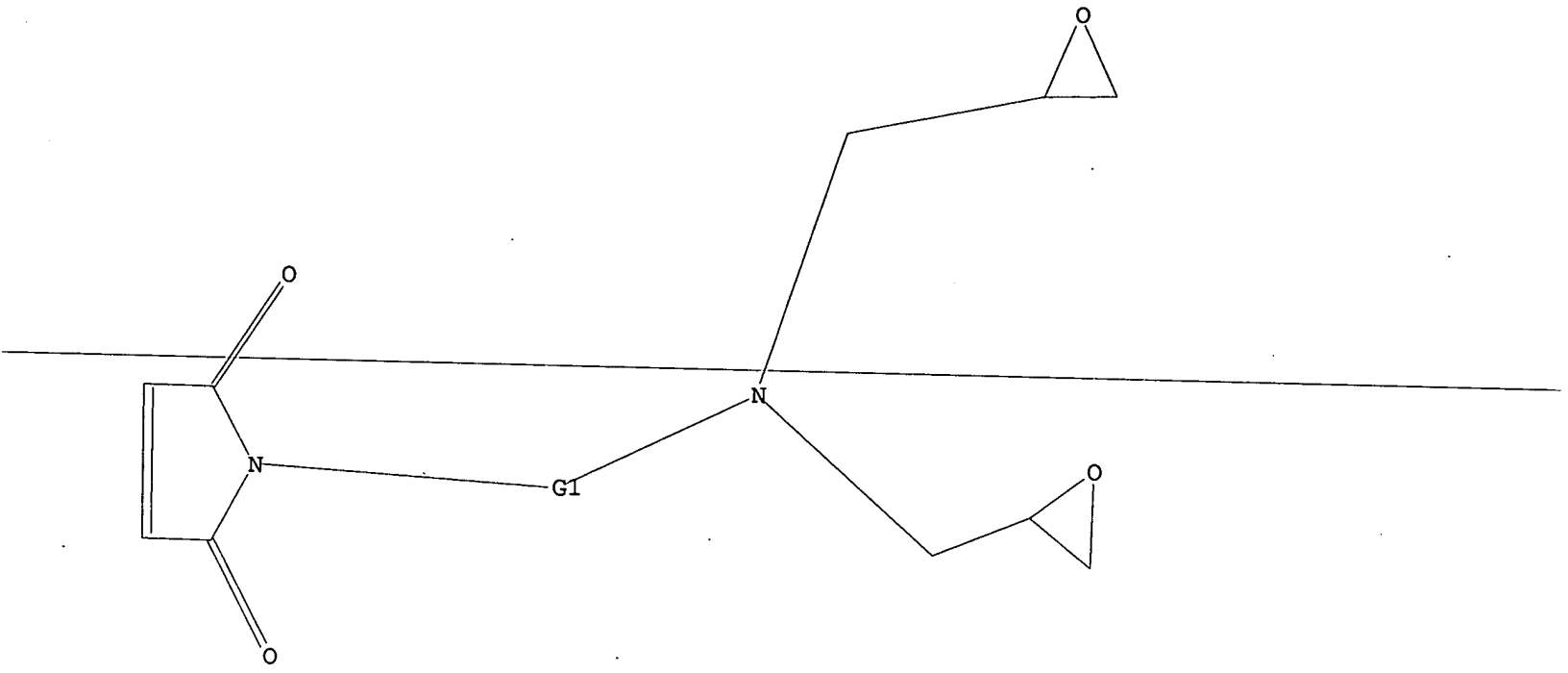
G1:Cy,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:Atom 9:Atom 10:Atom
11:CLASS 12:CLASS 13:Atom 14:Atom 15:Atom 16:CLASS 19:CLASS

L4 STRUCTURE UPLOADED

=> d
L4 HAS NO ANSWERS

L4 STR



G1 Cy,Ak

Structure attributes must be viewed using STN Express query preparation.

```
=> s L1
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SAMPLE SCREEN SEARCH COMPLETED -     39 TO ITERATE

100.0% PROCESSED      39 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          406 TO     1154
PROJECTED ANSWERS:               0 TO        0

L5            0 SEA SSS SAM L1

=> s L4
SAMPLE SEARCH INITIATED 11:30:10 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      3 TO ITERATE

100.0% PROCESSED       3 ITERATIONS                              0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            3 TO      163
PROJECTED ANSWERS:               0 TO        0

L6            0 SEA SSS SAM L4

=> s L4 full
FULL SEARCH INITIATED 11:30:17 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -    109 TO ITERATE
```

100.0% PROCESSED 109 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

L7 0 SEA SSS FUL L4

=> fil caplus caold; sL4
COST IN U.S. DOLLARS SINCE FILE ENTRY 316.72 TOTAL SESSION 316.93

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 11:30:58 ON 19 NOV 2004
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"HELP COMMANDS" at an arrow prompt (=>).

=> fil caplus caold; s L4
COST IN U.S. DOLLARS SINCE FILE ENTRY 0.86 TOTAL SESSION 317.79

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 11:31:07 ON 19 NOV 2004
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The logic expression entered contains L#s or saved query names which correspond to structures built by the STRUCTURE command or to screen sets. These must be searched in a substance file such as the REGISTRY file. In some files you may use a Registry Number answer set from a structure search as a search term or profile in some bibliographic file containing Registry Numbers, e.g. the CA file. For an explanation, enter "HELP CROSSOVER" at an arrow prompt (=>).

=> s L7
L8 0 L7

=> s oxiran? and pyrrol? and dione?
L9 63 OXIRAN? AND PYRROL? AND DIONE?

=> d ti

L9 ANSWER 1 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of indazoles and related compounds as p38 inhibitors

=> d ti 1 - 63

'-' IS NOT A VALID FORMAT FOR FILE 'CAPLUS'

The following are valid formats:

ABS --------- GI and AB
ALL --------- BIB, AB, IND, RE
APPS -------- AI, PRAI
BIB --------- AN, plus Bibliographic Data and PI table (default)
CAN --------- List of CA abstract numbers without answer numbers
CBIB -------- AN, plus Compressed Bibliographic Data
DALL -------- ALL, delimited (end of each field identified)
DMAX -------- MAX, delimited for post-processing
FAM --------- AN, PI and PRAI in table, plus Patent Family data
FBIB -------- AN, BIB, plus Patent FAM
IND --------- Indexing data
IPC --------- International Patent Classifications
MAX --------- ALL, plus Patent FAM, RE
PATS -------- PI, SO
SAM --------- CC, SX, TI, ST, IT
SCAN -------- CC, SX, TI, ST, IT (random display, no answer numbers;
              SCAN must be entered on the same line as the DISPLAY,
              e.g., D SCAN or DISPLAY SCAN)
STD --------- BIB, IPC, and NCL

IABS -------- ABS, indented with text labels
IALL -------- ALL, indented with text labels
IBIB -------- BIB, indented with text labels
IMAX -------- MAX, indented with text labels
ISTD -------- STD, indented with text labels

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

HIT --------- Fields containing hit terms
HITIND ------ IC, ICA, ICI, NCL, CC and index field (ST and IT)
              containing hit terms
HITRN ------- HIT RN and its text modification
HITSTR ------ HIT RN, its text modification, its CA index name, and
              its structure diagram
HITSEQ ------ HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
FHITSTR ----- First HIT RN, its text modification, its CA index name, and
              its structure diagram
FHITSEQ ----- First HIT RN, its text modification, its CA index name, its
              structure diagram, plus NTE and SEQ fields
KWIC -------- Hit term plus 20 words on either side
OCC --------- Number of occurrence of hit term and field in which it occurs

To display a particular field or fields, enter the display field codes. For a list of the display field codes, enter HELP DFIELDS at an arrow prompt (=>). Examples of formats include: TI; TI,AU; BIB,ST; TI,IND; TI,SO. You may specify the format fields in any order and the information will be displayed in the same order as the format specification.

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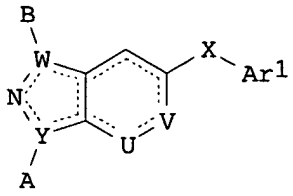
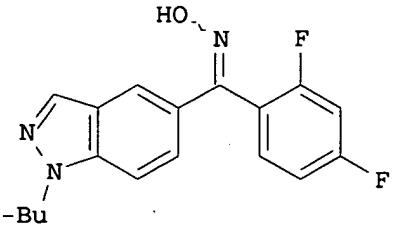
ENTER DISPLAY FORMAT (BIB):end

=> d L9 ti abs,ti

L9 ANSWER 1 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of indazoles and related compounds as p38 inhibitors
GI



I



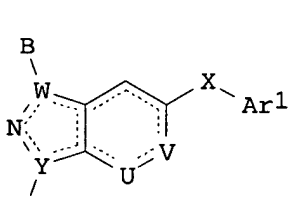
II

AB The invention provides for the preparation of the title compds. I [Y = C, N; W = C, N, S, provided that W = N, S, or O when Y = C, and W = C or N when Y = N; U = CH, N; V = C(E), N; X = O, S, SO, SO2, etc.; Ar1 = (un)substituted (hetero)aryl; A = H, OH, an amine protecting group, etc.; B = H, NH2, (un)substituted Me; E = H, OH, an amine protecting group, etc.; with the provisos; and stereoisomers, solvates, and pharmaceutically acceptable salts thereof] as p38 MAP kinase inhibitors. For example, cyclization of 4-bromo-2-methylaniline with NH4BF4 provided 5-bromo-1H-indazole, which was N-alkylated with 1-bromo-2-methylpropane (50.8% over 2 steps). Coupling with 2,4-difluorobenzaldehyde (69.1%), followed by oxidation (75.6%) and reaction with NH2OH•HCl (65.5%) gave (2,4-difluorophenyl)(1-isobutyl-1H-indazol-5-yl)methanone oxime (II). The latter inhibited p38α activity and LPS-induced TNF-α secretion from human peripheral blood mononuclear cells (PBMC) with IC50 values <500 nM. The invention also provides pharmaceutical compns. comprising I and methods of using the inhibitors and pharmaceutical compns. in the treatment and prevention of various disorders mediated by p38, such as inflammatory disease, autoimmune disease, destructive bone disorder, proliferative disorder, infectious disease, viral disease, or neurodegenerative disease (no data).

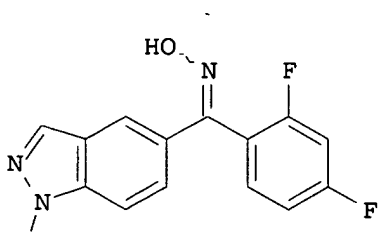
TI Preparation of indazoles and related compounds as p38 inhibitors

=> d L9 ti,abs 1-63

L9 ANSWER 1 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of indazoles and related compounds as p38 inhibitors
GI



I



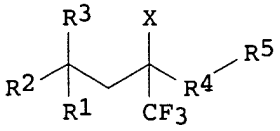
II

AB The invention provides for the preparation of the title compds. I [Y = C, N; W = C, N, S, provided that W = N, S, or O when Y = C, and W = C or N when Y = N; U = CH, N; V = C(E), N; X = O, S, SO, SO2, etc.; Ar1 = (un)substituted (hetero)aryl; A = H, OH, an amine protecting group, etc.; B = H, NH2, (un)substituted Me; E = H, OH, an amine protecting group, etc.; with the provisos; and stereoisomers, solvates, and pharmaceutically acceptable salts thereof] as p38 MAP kinase inhibitors. For example, cyclization of 4-bromo-2-methylaniline with NH4BF4 provided

5-bromo-1H-indazole, which was N-alkylated with 1-bromo-2-methylpropane (50.8% over 2 steps). Coupling with 2,4-difluorobenzaldehyde (69.1%), followed by oxidation (75.6%) and reaction with NH2OH•HCl (65.5%) gave (2,4-difluorophenyl)(1-isobutyl-1H-indazol-5-yl)methanone oxime (II). The latter inhibited p38α activity and LPS-induced TNF-α secretion from human peripheral blood mononuclear cells (PBMC) with IC50 values <500 nM. The invention also provides pharmaceutical compns. comprising I and methods of using the inhibitors and pharmaceutical compns. in the treatment and prevention of various disorders mediated by p38, such as inflammatory disease, autoimmune disease, destructive bone disorder, proliferative disorder, infectious disease, viral disease, or neurodegenerative disease (no data).

L9 ANSWER 2 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Using fragment chemistry data mining and probabilistic neural networks in screening chemicals for acute toxicity to the fathead minnow
AB The paper is illustrating how the general data mining methodol. may be adapted to provide solns. to the problem of high throughput virtual screening of organic chems. for possible acute toxicity to the fathead minnow fish. The present approach involves mining fragment information from chemical structures and is using probabilistic neural networks to model the relationship between structure and toxicity. Probabilistic neural networks implement a special class of multivariate non-linear Bayesian statistical models. The math. principles supporting their use for value prediction purposes are clarified and their peculiarities discussed. As part of the research phase of the data mining process, a dataset consisting of 800 structures and associated fathead minnow (Pimephales promelas) 96-h LC50 acute toxicity endpoint information is used for both the purpose of identifying an advantageous combination of fragment descriptors and for training the neural networks. As a result, two powerful models are generated. Model 1 implements the basic PNN with Gaussian kernel (statistical corrections included) while Model 2 implements the PNN with Gaussian kernel and separated variables. External validation is performed using a sep. dataset consisting of 86 structures and associated toxicity information. Both learning and generalization capabilities of the two models are investigated and their limitations discussed.

L9 ANSWER 3 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of propanol and propylamine derivatives and their use as glucocorticoid ligands
GI



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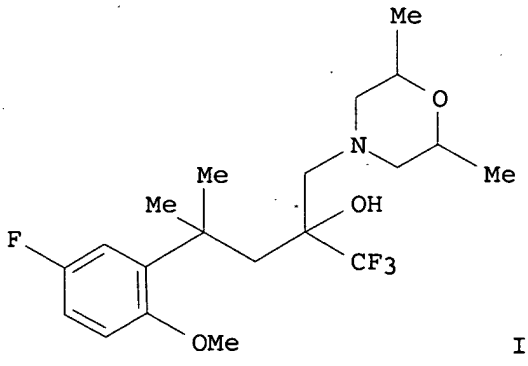


II

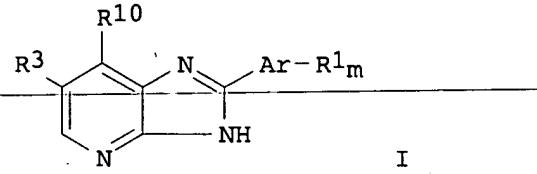
AB Title compds. I [R1 = (hetero)aryl, cycloalkyl, etc.; R2-3 = H, alkyl, arylalkyl, etc.; R4 = CO, divalent alkyl; R5 = **pyrrolidine**, morpholine, thiomorpholine, etc.; X = OH, amino] are prepared For instance,

2-hydroxy-4-methyl-2-trifluoromethylpent-4-enoic acid Et ester (preparation given) is alkylated with 4-fluoroanisole (AlCl3); the resulting ester is reduced to the diol (LAH), converted to the **oxirane** (CH2Cl2, pyridine, MsCl) and treated with 2,6-dimethylmorpholine (DMF, 100°) to give II. I are glucocorticoid receptor modulators and are useful for the treatment of inflammatory disorders.

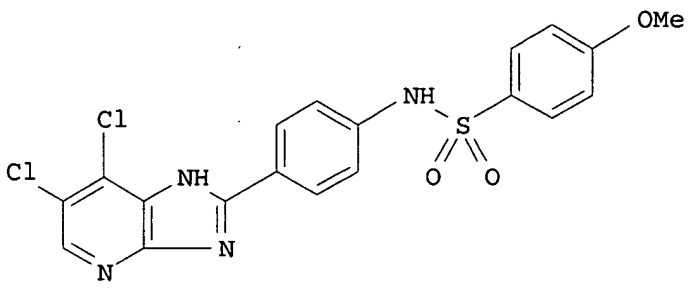
L9 ANSWER 4 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of imidazopyridines as Itk kinase inhibitors for use against asthma and allergic rhinitis

GI



I



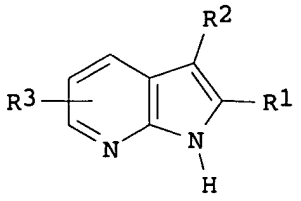
II

AB The use of imidazopyridines (shown as I; variables defined below; e.g. II trifluoroacetate) and pharmaceutically acceptable salts thereof in the manufacture of a medicament for the treatment or prophylaxis of diseases or conditions in which inhibition of kinase Itk activity is beneficial is disclosed. Certain novel compds. I, together with processes for their preparation, compns. containing them and their use in therapy are also disclosed.

For I: R3 = halogen, CN, C1-3-alkyl or C1-3-alkoxy; Ar = Ph, a 5-6-membered heteroarom. ring or an indole ring, said heteroarom. ring incorporating 1 to 3 O, N and S; R1 = H, halogen, CN, C1-6-alkyl, NO2, SO2Me, C1-6-alkynyl, CH2OH, OR2, (CH2)nNR4R5 or Ph (un)substituted by NH2; m = 1-2 and when m = 2, each R1 may be selected independently; n = 0 or 1; R10 = H, halogen, CN, C1-4-alkyl, C1-4-alkoxy, NR14R15 or a group -X-Y-Z (X = O, S, a bond or NR16 wherein R16 = H or C1-4-alkyl; Y = C1-4-alkyl or a bond; Z = Ph, naphthyl or a 5- or 6-membered heteroarom. ring, a 5- or 6-membered saturated heterocyclic ring containing 1-2 heteroatoms = O, N and S, or C3-6-cycloalkyl); addnl. details are given in the claims. Methods of preparation are claimed and >250 example prepns. of I are included. For example, II was prepared by condensing 4-(6,7-dichloro-1H-imidazo[4,5-b]pyridin-2-yl)aniline with 4-methoxybenzenesulfonyl chloride in pyridine. In another example, 5-bromo-2,3-diaminopyridine was cyclized with 4-hydroxybenzaldehyde in DMF in the presence of iron(III) chloride hexahydrate to give 65% 4-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)phenol. In another example, N-benzyl-5-(6-bromo-3H-imidazo[4,5-b]pyridin-2-yl)pyridin-2-amine bis(trifluoroacetate) was prepared in 3 steps starting with cyclization of 2,3-diamino-5-bromopyridine with 6-chloronicotinic acid in the presence of polyphosphoric acid (53%) followed by chlorination using POCl3 to give 44% 6-bromo-2-(6-chloropyridin-3-yl)-3H-imidazo[4,5-b]pyridine followed by condensation with benzylamine (51%). Compds. of Examples 1 to 278 gave IC50 values for inhibition of Itk activity of <25

μM, e.g. 0.26 μM for II.

L9 ANSWER 5 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of substituted **pyrrolopyridines** as Itk kinase inhibitors
GI

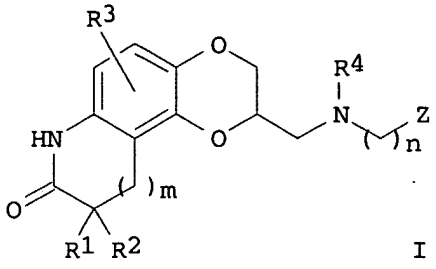


I

AB The title compds. [I; R1 = (un)substituted Ph, 5-6 membered aromatic heterocyclyl containing 1-3 heteroatoms selected from O, S and N; R2 = (un)substituted Ph, 5-6 membered aromatic heterocyclyl containing 1-3 heteroatoms selected from O, S and N; R3 = H, halo, alkyl, alkoxy, CN] and their salts, useful for treating or reducing the risk of a human disease or condition in which inhibition of Itk kinase activity is beneficial (such as asthma and allergic rhinitis), were prepared Thus, reacting 2-(4-methoxyphenyl)-1-phenylethanone with 5-bromo-2-hydrazinopyridine at 230° afforded 58% 5-bromo-3-(4-methoxyphenyl)-2-phenyl-1H-**pyrrolo**[2,3-b]pyridine. The exemplified compds. I showed IC50 of < 25 μM against Itk kinase. The pharmaceutical composition comprising the compound I is claimed.

L9 ANSWER 6 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI A highly flexible route to 1,2,3,4,5,6-hexahydro-5-hydroxypyrimidin-2-ones as potential HIV protease inhibitors
AB The first asym. synthesis of 1,2,3,4,5,6-hexahydro-5-hydroxypyrimidin-2-ones as potential HIV protease inhibitors of is described. Key step of the synthesis is an auxiliary based stereoselective alkylation by means of the (R)-1-amino-2-methoxymethylpyrrolidine (RAMP)/(S)-1-amino-2-methoxymethylpyrrolidine (SAMP)-hydrazone method starting from a readily available key building block, pyrimidin-2,5-**dione.** The synthesis is short and highly versatile in the choice of the substitution pattern as well as the absolute configuration of the alkylated 1,2,3,4,5,6-hexahydro-5-hydroxypyrimidin-2-ones. The biol. and pharmacol. activity of the compds. thus prepared was not reported.

L9 ANSWER 7 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Dioxino-fused indolone and quinolinone derivatives and their preparation, pharmaceutical compositions, and use as dopamine agonists, e.g., as antipsychotics
GI



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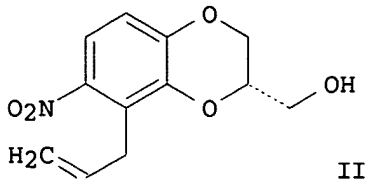
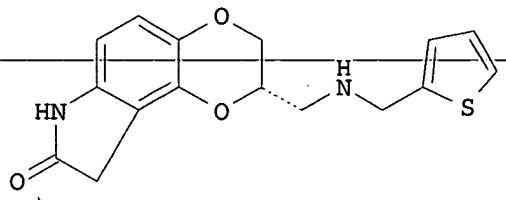


II



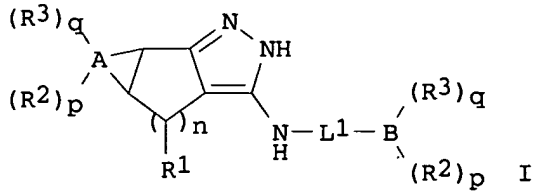
III

AB Title compds. I are disclosed [wherein: R1, R2 = H, alkyl, Ph, or PhCH2; or R1R2 = alkylidene, R3-(un)substituted benzylidene, oxo, or cyclic alkylene group; R3 = H, OH, halo, CF3, CF3O, alkyl, alkoxy, aralkoxy, alkanoyloxy, (di)(alkyl)amino, alkanamido, or alkanesulfonamido; R4 = H or alkyl; m = 0, 1, 2; n = 0-6, inclusive; Z = H, OH, alk(en/yn)yl, alkoxy, cycloalkyl, polycycloalkyl, R3-(un)substituted Ph, PhO, naphthyl, naphthyloxy, heteroaryl, or heteroaryloxy (heterocyclic ring = thiophene, furan, pyridine, pyrazine, pyrimidine, indole, indazole, imidazole, chroman, coumarin, carbostyril, quinoline, benzisoxazole, benzoxazole, pyrazole, **pyrrole**, thiazole, oxazole, or isoxazole); or a pharmaceutically acceptable salt thereof]. I are dopamine autoreceptor agonists, modulating synthesis and release of dopamine. I also act as partial agonists at the postsynaptic dopamine D2 receptor, and are capable of functioning as either agonists or antagonists depending on the level of dopaminergic stimulation. I are thus useful for treating disorders of the dopaminergic system, including schizophrenia, schizoaffective disorder, Parkinson's disease, Tourette's syndrome, and hyperprolactinemia. Approx. 46 compds. I were prepared, mostly as (S)-isomers, and isolated as fumarate salts; the non-stereochem. free bases are also claimed. Prepns. of several intermediates are also given. For instance, 5-nitroguaiacol Na salt was O-allylated, O-demethylated, etherified with (R)-glycidyl tosylate, and rearranged with concomitant internal etherification to give (S)-isomeric intermediate II. This compound underwent O-tosylation, permanganate oxidation of the allyl sidechain to an acid, hydrogenation of the nitro group to amino, cyclization of the amine with the acid to give a lactam, and aminolysis of the tosylate by thiophene-2-methylamine, to give invention compound III, isolated as the monofumarate. In a test for displacement of [3H]-quinpirole from rat striatal D2 receptors in vitro, III had an IC50 of 0.51 nM. In a hypolocomotion assay for antipsychotic activity in mice, III had an ED50 value of 0.0005 mg/kg s.c. A representative compound, the analog of III with Z = Ph, inhibited dopa accumulation in rats by 67.5% at 10 mg/kg s.c., indicating activity as a dopamine autoreceptor agonist.

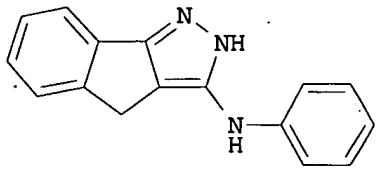
L9 ANSWER 8 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of N-substituted tricyclic 3-aminopyrazoles as PDGF receptor inhibitors for treatment of tumors and other cell proliferation disorders

GI



I



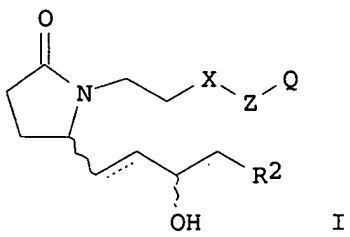
II

AB Title compds. I [wherein n = 1-4; R1 = H, alkyl, OH, alkoxy, O, NH2, or (di)alkylamino; A = aryl, optionally benzo-fused heteroaryl or (hetero)cycloalkyl; p = 0-2; R2 = XA1D or XA1YA2; X and Y = independently absent, O, S, SO, SO2, OCO, CO2, OCO2, or optionally alkyl substituted NH, NHCO, CONH, NHCO2, OCONH, NHCONH, NHSO2, or SO2NH; A1 = absent or (un)substituted alkyl or alkenyl, A2 = H or (un)substituted alkyl or alkenyl; D = (un)substituted, optionally benzo-fused (hetero)aryl, (hetero)cycloalkyl, or carbocyclyl; q = 0-4; R3 = halo, OH, NH2, S, NO2, CN, (halo)alkyl, (halo)alkoxy, (halo)thioalkyl, (halo)sulfonylalkyl, or optionally alkyl substituted NH2, NHCO-alkyl, NHCONH2, OCONH2, NHCO2-alkyl, NHSO2-alkyl, OCONH2; L1 = absent or alkyl; B = (hetero)aryl or optionally benzo-fused (hetero)cycloalkyl; with the proviso that p + q = 0-4; or optical isomers, enantiomers, diastereomers, racemates, or pharmaceutically acceptable salts thereof] were prepared as inhibitors of platelet-derived growth factor receptor (PDGF-R) kinase. Examples include synthetic methods and bioassays of inhibition of PDGF-R kinase and c-Abl kinase activity, suppression of cell proliferation, antitumor activity, cell viability evaluation by growth phases, effects of combination radiotherapy, and drug bioavailability of prodrugs of representative compds. of the invention. For instance, coupling of indan-1-one with phenylisothiocyanate in the presence of NaH in THF to give 1-oxoindan-2-carbothioic acid phenylamide, followed by cyclization with hydrazine in EtOH provided (2,4-dihydroindeno[1,2-c]pyrazol-3-yl)phenylamine (II). The latter inhibited PDGF-R by 91% with an IC50 value of 0.317 μM. Thus, I and their pharmaceutical compns. are useful for the treatment of conditions, such as tumors and other cell proliferative disorders.

L9 ANSWER 9 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of hydroxyorgano **pyrrolidinones** as EP4 receptor selective agonists for the treatment of hypertension and other disorders

GI



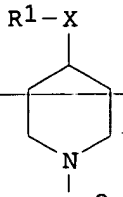
I

AB This invention is directed to hydroxyorgano **pyrrolidinones** (I;

e.g. 4-[3-[2-(3-hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]propyl]benzoic acid; R2, X, Z and Q are defined below and in more detail in the claims) that are EP4 receptor selective prostaglandin agonists. This invention is also directed to pharmaceutical compns. containing those compds. This invention is also directed to methods of treating hypertension, liver failure, loss of patency of the ductus arteriosus, glaucoma or ocular hypertension. IC50 values for binding of 5-[3-[2S-[3R-hydroxy-4-(3-trifluoromethylphenyl)butyl]-5-oxopyrrolidin-1-yl]propyl]thiophene-2-carboxylic acid (II) to various receptors are human EP1 receptor, >1000 nm; rat EP2 receptor, 463 nm; human EP3 receptor, > 1000 nm; and rat EP4 receptor, 11 nm. II exhibited an EC50 value of 0.6 nm in an assay involving cAMP elevation in 293S cell lines stably overexpressing recombinant rat EP4 receptors. Results are also presented for the hypotensive effect of the Na salt of II in in vivo rabbit and primate models. In I, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt: the dotted line is a bond or no bond; X is =CH2- or O; Z is -(CH2)3-, thienyl, thiazolyl or Ph, provided that when X is O, then Z is phenyl; Q is carboxy, (C1-C4)alkoxycarbonyl or tetrazolyl; R2 is -Ar or -Ar1-V-Ar2; V is a bond, -O-, -OCH2- or -CH2O-. Ar is a partially saturated, fully saturated or fully unsatd. 5-8 membered ring optionally having 1-4 heteroatoms selected independently from O, S and N, or a bicyclic ring consisting of two fused independently partially saturated, fully saturated or fully unsatd. 5-6 membered rings, taken independently, optionally having 1-4 heteroatoms selected independently from N, S and O, said partially or fully saturated ring or bicyclic ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar1 and Ar2 are each independently a partially saturated, fully saturated or fully unsatd. 5-8 membered ring optionally having 1-4 heteroatoms selected independently from O, S and N, said partially or fully saturated ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar is optionally substituted on C or N, on one ring if the moiety is monocyclic, or on one or both rings if the moiety is bicyclic, with up to three substituents per ring each independently selected from hydroxy, halo, carboxy, (C1-C7) alkoxy, (C1-C4)alkoxy(C1-C4)alkyl, (C1-C7)alkyl, (C2-C7)alkenyl, (C3-C7)cycloalkyl, (C3-C7)cycloalkyl(C1-C4)alkyl, (C3-C7)cycloalkyl(C1-C4)alkanoyl, formyl, (C1-C8) alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylamino, (C1-C4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylamino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N- or di-N,N-(C1-C4)alkylamino, carbamoyl, mono-N- or di-N,N-(C1-C4)alkylcarbamoyl, cyano, thiol, (C1-C6)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar are optionally substituted on C with up to three fluoro. Ar1 and Ar2 are independently optionally substituted on C or N with up to three substituents each independently selected from hydroxy, halo, carboxy, (C1-C7)alkoxy, (C1-C4)alkoxy(C1-C4)alkyl, (C1-C7)alkyl, (C2-C7)alkenyl, (C3-C7)cycloalkyl, (C3-C7)cycloalkyl(C1-C4)alkyl, (C3-C7)cycloalkyl(C1-C4)alkanoyl, formyl, (C1-C8)alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylamino, (C1-C4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylamino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N- or di-N,N-(C1-C4)alkylamino, carbamoyl, mono-N- or di-N,N-(C1-C4)alkylcarbamoyl, cyano, thiol, (C1-C6)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar1 and Ar2 are optionally substituted on C with up to three fluoro. (a) when X is (CH2)- and Z is -(CH2)3-, then R2 is not thienyl, Ph or Ph monosubstituted with chloro, fluoro, Ph, methoxy, trifluoromethyl or (C1-C4) alkyl; and (b) when X is (CH2)-, Z is -(CH2)3-, and Q is carboxy or (C1-C4) alkoxycarbonyl, then R2 is not (i)

(C5-C7)cycloalkyl or (ii)phenyl, thienyl or furyl each of which may be optionally monosubstituted or disubstituted by one or two substituents selected, independently in the latter case, from halogen atoms, alkyl groups having 1-3 C atoms which may be substituted by one or more halogen atoms, and alkoxy groups having 1-4 C atoms. Although the methods of preparation are not claimed, 41 example prepns. are included.

L9 ANSWER 10 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of piperidinyl alcohols as chemokine receptor modulators for treatment of diseases such as asthma
GI

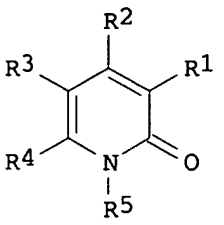


$CR^2R^3(CH_2)_mCR^4(OH)CR^5R^6(CR^7R^8)_nNR^{32}ZYR^9$ I

AB The invention provides piperidinyl alcs. (shown as I; variables defined below; e.g. N-[(2R)-3-[4-(3,4-dichlorophenoxy)piperidin-1-yl]-2-hydroxypropyl]-2-(methylsulfonyl)benzamide) for use as modulators of chemokine receptor (especially CCR3) activity for use in, for example, treating asthma. For I: X is CH2, O, S(O)2 or NR10; Y is a bond, CH2, NR35, CH2NH, CH2NHC(O), CH(OH), CH(NHCOR33), CH(NHSO2R34), CH2O or CH2S; Z is C(O), or when Y is a bond Z can also be S(O)2; R1 is (un)substituted aryl, (un)substituted heterocyclyl or C4-6 cycloalkyl fused to a benzene ring; addnl. details are given in the claims. Percent inhibition at 3 nM eotaxin of eotaxin-mediated human eosinophil chemotaxis is tabulated for 16 examples of I, e.g. 106 % for N-[(2R)-3-[4-(3,4-dichlorophenoxy)piperidin-1-yl]-2-hydroxypropyl]-1-oxo-1,2-dihydroisoquinoline-4-carboxamide. Histamine H1 receptor binding activity was determined for the same compds., e.g. pKi = 8.4 for N-[(2R)-3-[4-(3,4-dichlorophenoxy)piperidin-1-yl]-2-hydroxypropyl]-1-oxo-1,2-dihydroisoquinoline-4-carboxamide. 49 Example prepns. of intermediates and 234 of I are included. For example, to prepare N-[(2R)-3-[4-(3,4-Dichlorophenoxy)piperidin-1-yl]-2-hydroxypropyl]-2-(methylsulfonyl)benzamide (0.055 g), a mixture of 2-(methylsulfonyl)benzoic acid (0.063 g), (2R)-1-amino-3-[4-(3,4-dichlorophenoxy)piperidin-1-yl]propan-2-ol (0.1 g) and N,N-diisopropylethylamine (0.1 mL) in dry DMF (3 mL) was cooled to 0° with stirring; 2-(1H-9-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (0.13 g) was added and the mixture was stirred at 0° for 1-2 h. The invention also provides a process for making 4-(3,4-dichlorophenoxy)piperidine, which is useful as an intermediate for making certain compds. of the invention. The process comprises (a) reacting 4-hydroxypiperidine with a suitable base in a suitable solvent at room temperature; and (b) heating the mixture so produced and

1,2-dichloro-4-fluorobenzene at 50-90°, or at reflux of the solvent used.

L9 ANSWER 11 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of substituted pyridinones as modulators of p38 MAP kinase
GI



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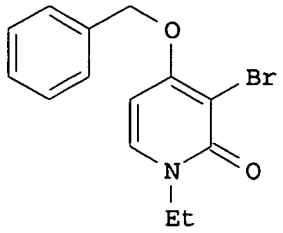


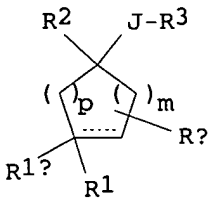
II

AB Disclosed are title compds. I [wherein R1 = H, halo, NO2, CHO, CN, CO2H, or (un)substituted (halo)alkyl, (aryl)alkoxy, aryl(alkyl), alkenyl, (aryl)alkynyl, (aryl)alkanoyl, alkoxyalkyl, or haloalkoxy; R2 = H, OH, halo, NR8R9, CO2R, or (un)substituted OSO2-alkyl, OSO2-aryl, arylalkoxy, aryloxy(alkyl), arylthio(alkoxy), arylalkynyl, alkoxy(alkoxy), alkyl, alkynyl, OCONH(CH2)n-aryl, OCON(alkyl)(CH2)n-aryl, dialkylamino, (hetero)aryl(alkyl), arylalkenyl, or heterocycloalkyl(alkyl); R3 = H, halo, alkenyl, NR6R7, NR6R7-alkyl, alkyl, or (un)substituted (aryl)alkoxycarbonyl, aryloxycarbonyl, arylalkyl, OCONH(CH2)n-aryl, arylalkoxy, OCON(alkyl)(CH2)n-aryl, aryloxy, arylthio, or (aryl)thioalkoxy; R4 = H or (un)substituted alkyl; R5 = H, aryl, aryl(thio)alkyl, NH2, alkoxycarbonyl, alkynyl, SO2-alkyl, (hetero)cycloalkyl(alkyl), heteroaryl, or (un)substituted alkyl, alkoxy(alkyl), or alkenyl; R6 and R7 = independently H, OH, or (un)substituted (aryl)alkyl, alkoxy(alkyl), alkanoyl(alkyl), arylalkoxy, SO2-alkyl, (aryl)alkoxycarbonyl, heteroarylalkyl, or arylalkanoyl; or NR6R7 = (un)substituted (thio)morpholinyl, **pyrrolidinyl**, piperidinyl, **pyrrolidinyl**, or piperazinyl; R8 = independently H or (un)substituted (aryl)alkyl or (aryl)alkanoyl; R9 = H or (un)substituted (aryl)alkyl, (aryl)alkanoyl, cycloalkyl(alkyl), alkenyl, heteroaryl, (alkyl)aminoalkyl, SO2Ph, or aryl; R = independently H or (un)substituted alkyl; n = 0-6; and pharmaceutically acceptable salts thereof]. These compds. are useful for treating diseases and conditions caused or exacerbated by unregulated p38 MAP Kinase and/or TNF activity, such as inflammation, ischemia, viral infections, and autoimmune diseases (no data). Pharmaceutical compns. containing I, methods of preparing them, and methods of treatment using the compds. are also disclosed. For example, reaction of 4-benzyloxy-2(1H)-pyridone with EtBr in the presence of K2CO3 in DMF gave II. The latter inhibited MKK6-activated human p38α kinase phosphorylation of a biotinylated substrate or human p38α-induced phosphorylation of EGFRP (epidermal growth factor receptor peptide) with an IC50 in the range of 1 μM to 25 μM.

L9 ANSWER 12 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of cycloalkyl inhibitors of potassium channel function for preventing/treating arrhythmia and IKur-associated conditions

GI



AB Claimed are novel cycloalkyl compds. (shown as I; variables defined below; e.g. cis- and trans-N-(4-hydroxy-1-thiophen-2-ylcyclohexylmethyl)-2-methoxybenzamide and trans-N-[[4-[N'-cyano-N''-ethyl-N-(furan-2-ylmethyl)guanidino]-1-phenylcyclohexyl]methyl]-2-methoxybenzamide) useful

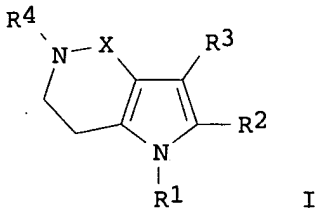
as inhibitors of K channel function (especially inhibitors of the Kv1 subfamily of voltage gated K+ channels, especially inhibitors Kv1.5 which was linked to the ultra-rapidly activating delayed rectifier K+ current IKur; no data), methods of using such compds. in the prevention and treatment of arrhythmia and IKur-associated conditions, and pharmaceutical compns. containing
such compds. For I: dashed line = an optional double bond, provided that R1a is absent when a double bond is present; m and p = 0-3; R1 = H, NR8C(:W)NR6R7 (W = NR8a2, NCO2R8a2, NC(O)R8a2, NCN, NSO2R8a2), NR8SO2NR6R7, etc.; R1a = H, RX; or R1 and R1a together form oxo; or R1 and R1a together with the C atom to which they are attached combine to form an (un)substituted spiro-fused heterocyclo group; or R1 and R1a together combine to form :CR8R9. R2 is heteroaryl, (heteroaryl)alkyl, aryl, (aryl)alkyl, heterocyclo, (heterocyclo)alkyl, alkyl, alkenyl or cycloalkyl; J is a bond, C1-4 alkylene or C1-4 alkenylene; R3 = R5 (R5 = NR6aR7a, heteroaryl, (heteroaryl)alkyl, aryl, arylalkyl, alkyl, etc.), OR5, C(:Z1)R5, OC(:Z1)R5, C(:Z1)OR5, NR8a1C(:Z1)R5, etc.; RX is one or more optional substituents, attached to any available ring carbon atom; addnl. details including provisos are given in the claims. Although the methods of preparation are not claimed, >600 example prepns. are included.

L9 ANSWER 13 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of vanilloid receptor ligands and their use in treatments
AB Claimed are compds. having the general structure R1CR2:CR3C(:X)YR4 or R1R2CHCR3R3C(:X)YR4 (I; variables defined below; e.g. (2E)-3-[4-(tert-butyl)phenyl]-N-phenylprop-2-enamide and (2,3-dihydrobenzo[1,4]dioxin-6-yl)[4-(4-dimethylaminophenyl)pyridin-2-yl]amine) and compns. containing them, for the treatment of acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and nonvascular syndromes, tension headache, , general inflammation arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders,inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathy pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentiation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders. I are thought to be vanilloid receptor ligands, but no test data are provided. Although the methods of preparation are not claimed, .apprx.130 example prepns. and characterization data for .apprx.400 I are included. For I: R1 is Ph, naphthyl or (un)saturated 5- or 6-membered ring heterocycle; R2 is H, hydroxy, halo, C1-6alkyl, or (un)saturated 5- or 6-membered ring heterocycle; or R1 and R2 together are o-benzenediyl-L1-o-benzenediyl. R3 is H or C1-4alkyl; or R1 and R3 together are o-benzenediyl-L2- or -Z-L2- (Z = pyridine-2,3-diyl). R4 is Ph, (un)saturated 5- or 6-membered ring heterocycle, 10-membered bicyclic ring comprising fused 6-membered rings, containing 0-4 N atoms with the remainder being C atoms, with at least one of the 6-membered rings being aromatic; X is O, S or NRa; or X and R2 together are :N-CH:CH-, :C-O-, :C-S-, or :C-NRa-; Y is NH or O; addnl. details including provisos are given in the claims.

L9 ANSWER 14 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Cycloaddition reaction of epoxides with various alkenes under microwave irradiation
AB The reactivity of gem-dicyano epoxides with various alkenes is studies in solvent free conditions, and in homogeneous solution, under microwave irradiation
Reactants included 3-phenyl-2,2-**oxiranedicarbonitrile**, 3-(4-methoxyphenyl)-2,2-**oxiranedicarbonitrile**,

3-(4-chlorophenyl)-2,2-**oxiranedicarbonitrile**, 3-(4-nitrophenyl)-2,2-**oxiranedicarbonitrile.** Microwave heating of these substrates in solvent, yields carbonyl ylides which give 1-3-dipolar cycloaddn. For example, the reaction of 3-phenyl-2,2-**oxiranedicarbonitrile** with (2E)-2-butenedioic acid di-Me ester gave 2,2-dicyanotetrahydro-5-phenyl-3,4-furandicarboxylic acid di-Me ester. The reaction of 3-phenyl-2,2-**oxiranedicarbonitrile** with 1-phenyl-1H-**pyrrole**-2,5-**dione** gave hexahydro-4,6-dioxo-3,5-diphenylfuro[3,4-c]**pyrrole** -1,1-dicarbonitrile.

L9 ANSWER 15 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation and use of 1,5,6,7-tetrahydropyrrolo[3,2-c]pyridine derivatives for treatment of obesity
GI



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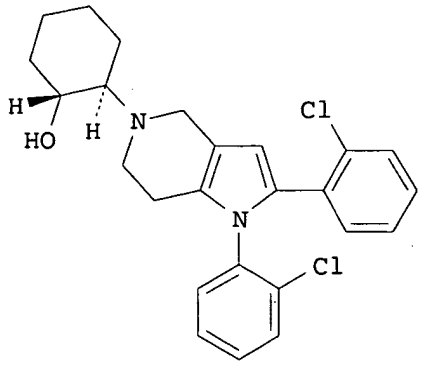
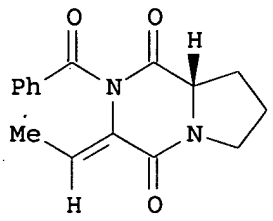


II

AB Title compds. I [R1 = (un)substituted phenyl; R2 = H, halo, alkyl, Ph, etc.; R3 = H, alkyl, benzyl; X = CO, CH2, provided that when X = CO, R4 = H, alkyl, etc. and when X = CH2, R4 = alkyl, cycloalkyl, 2-hydroxy-1-Pr, etc.] are prepared Data for over 150 synthetic examples are provided. For instance, trans-2-[1-[2-chlorophenyl]-2-[4-chlorophenyl]-1,4,6,7-tetrahydro-5H-**pyrrolo**[3,2-c]pyridin-5-yl]cyclohexanol (II) is prepared using a late-stage **pyrrole** forming step. II•HCl at 10 mg/kg p.o. reduced food consumption (relative to the food consumption observed for the vehicle control group) by 33% to 44 % when measured at time points from 30 to 240 min in a fasted-refed assay (rat). .I are useful to suppress appetite, induce weight loss and treat obesity.

L9 ANSWER 16 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Stereoselective epoxidation and bromoalkoxylation with 3-ylidenepyrazine-2,5-**diones**
GI



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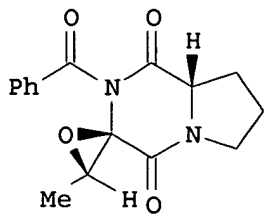

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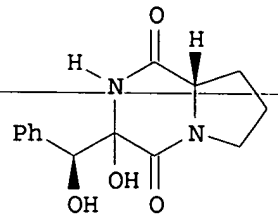
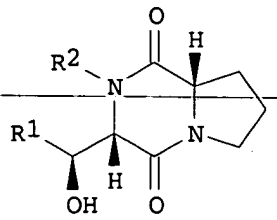


III



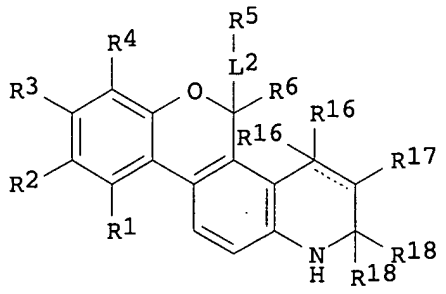
IV

AB 3-Ylidenepyrazine-2,5-**diones**, e.g., I, were stereoselectively epoxidized by dimethyldioxirane giving access to spirooxiranes, e.g., II, and diols, e.g., III. Bromohydroxylation and bromoalkoxylation of 3-ylidenepyrazine-2,5-**diones** produced high yields of optically active 3-(1-bromoalkyl)pyrazine-2,5-**diones** with a 3-hydroxy or 3-alkoxy function, resp. Whereas direct hydrogenation of epoxides afforded epimeric mixts. of 3-(1-hydroxyalkyl)pyrazine-2,5-**diones**, the highly stereoselective transformation into IV (R1 = Me, i-Pr, R2 = PhCO; R1 = Ph, R2 = H)was possible by primary acid cleavage of the **oxirane** ring followed by hydrogenation of the resulting keto-enol mixts.

L9 ANSWER 17 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of glucocorticoid-selective benzopyrano[3,4-f]quinolines as antiinflammatory agents

GI



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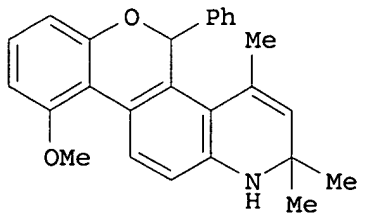


II

AB Title compds. I [R1 = L1RA; L1 = a bond, O, S, SO, SO2, CO, CS, CO2, OCO, or (un)substituted amino, NHCO, CONH, SO2NH, NHSO2, etc.; RA = OH, SH, CO2H, alkoxycarbonyl, CN, halo(alkoxy), CHO, alkyl, alkenyl, alkynyl, or (un)substituted amino, CONH2, etc.; R2-4 = H, R1 or R1-2 taken together may form methylenedioxy, etc.; L2 = bond, alkynylene, CO, CS, O, S, SO, SO2, (un)substituted alkylene, amino, etc.; R5 = H, halo, CN, (cyclo)alkyl, alkynyl, heterocyclyl, aryl, etc.; R6 = H, alkyl, L2R5 and R6 together may form :O, (un)substituted carbocyclic ring, heterocyclic ring, or alkylidene; R16 = H, alkyl or 2 R16 together form an alkenyl; Y = C, N, or NO; R17 = absent or H or alkyl; R18 = independently H or alkyl; or 2 R18 together form a heterocyclic ring or carbocyclic ring] are prepared

as antiinflammatory agents. For example, 2,6-dimethoxyphenylboronic acid (preparation given) is coupled with Me 2-bromo-5-nitrobenzoate using Cs2CO3 and Pd(PPh3)2Cl2 in DMF. The product is demethylated with BBr3 to give the hydroxylactone. Methylation with MeI in Cs2CO3, followed by Pd/C catalyzed reduction, affords 8-amino-1-methoxy-6H-dibenzo[b,d]pyran-6-one. Skraup ring annulation provides the benzopyrano[3,4-f]quinoline, which is functionalized using PhLi and deoxygenated with BF3•OEt2 and SiEt3H to II. The latter selectively inhibits binding with the human glucocorticoid receptor compared to the progesterone receptor with Ki values of 8.6 and 10,000, resp. I are useful for partially or fully antagonizing, repressing, agonizing, or modulating the glucocorticoid receptor and treating immune, autoimmune, and inflammatory diseases in a mammal. Also disclosed are pharmaceutical compns. comprising I and methods of inhibiting immune or autoimmune diseases in a mammal.

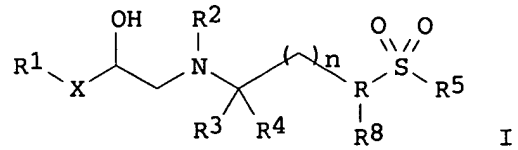
L9 ANSWER 18 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Product class 10: organometallic complexes of titanium
AB A review of application and preparation of organometallic complexes of titanium. These complexes are useful as catalysts in organic synthesis and for preparation of polymers.

L9 ANSWER 19 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of substituted oxazolidinones for combinational therapy in the treatment and/or prophylaxis of thromboembolic diseases
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to combinations of (A) oxazolidinones I [R1 = 5-X-2-thienyl (X = Cl, Br, Me, CF3); R2 = DA; A = phenylene; D = 5- or 6-membered heterocyclic ring containing S, N or O; R4 - R8 = H], or their pharmaceutically acceptable salts, hydrates, prodrugs or their mixts. and (B) other pharmaceutically active ingredients; to a method for producing said combinations; and to the use thereof as medicaments, in particular for the treatment and/or prophylaxis of thrombo-embolic diseases. Thus, the claimed oxazolone II was prepared from epoxide III via epoxide ring opening with aniline derivative IV, cyclization with carbonyldiimidazole, and N-acylation with 5-chlorothiophene-2-sulfonyl chloride. II was tested for antithrombotic activity in the arteriovenous shunt model (Rat) after [ED50 = 3 mg/kg (p.o.); IC50 = 0.7 nM]; II had a synergistic effect when used in combination with clopidogrel.

L9 ANSWER 20 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Aromatic and heteroaromatic amino alcohol derivatives useful as β3 adrenergic agonists, for treatment of pollakiuria and urinary incontinence, and their preparation.
GI



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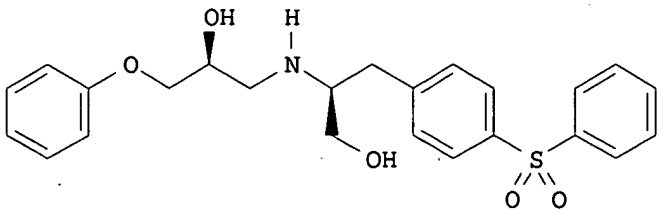
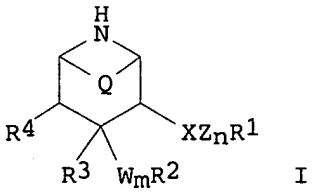


II

AB The invention relates to compds. I [wherein R1 is Ph, pyridyl, indolyl, or carbazolyl, each of which may be substituted with one or two substituent(s); R2 is hydrogen, an amino protective group, etc.; R3 and R4 are each independently hydrogen, lower alkyl or hydroxy(lower)alkyl; R is a benzene or pyridine nucleus; R5 is aryl, ar(lower)alkyl, heterocyclic, or alkyl, each of which may be substituted with one, two, or three substituent(s); R8 is hydrogen or halogen; X is a single bond or OCH2; and n is 0, 1, or 2] or salts thereof. I and their pharmaceutically acceptable salts are β3 adrenergic receptor agonists, useful for the prophylactic and/or therapeutic treatment of pollakiuria or urinary incontinence. Approx. 700 compds. were prepared as invention compds. and/or intermediates. For instance, tert-Bu [(S)-2-hydroxy-1-(4-hydroxybenzyl)ethyl]carbamate was protected with Me2C(OMe) as the oxazolidine, then converted to the aryl triflate, coupled with PhSH, oxidized to the sulfone, and deprotected to give (S)-2-amino-3-[4-(phenylsulfonyl)phenyl]-1-propanol as the hydrochloride. This compound underwent reductive N-benzylation with benzaldehyde, coupling with (S)-2-(phenoxymethyl)**oxirane**, and hydrogenolytic debenzylation, to give title compound II. When administered intraduodenally to anesthetized beagle dogs at 0.32 mg/kg, II gave a 30% inhibition of carbachol-induced (1.8 μg/kg) increase in intravesical pressure (IVP).

L9 ANSWER 21 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Product class 16: indolizines
AB A review describes some of the most useful methods for the synthesis of indolizines. The methods described are categorized as synthesis by ring-closure reactions; ring transformation; and substituent modification.

L9 ANSWER 22 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Methods of treating or preventing Alzheimer's disease using 4-aryl-3-aralkoxypiperidines and -azabicyclooctanes
GI



I

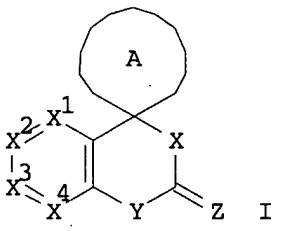
AB Disclosed are methods for treating or preventing Alzheimer's disease, and other diseases, and/or inhibiting β-secretase enzyme, and/or

inhibiting deposition of A beta peptide in a mammal, using 3,4-disubstituted piperidinyl compds. (I) wherein the variables R1, R2, R3, R4, Q, W, X, Z, m, and n are defined below. Although neither the compds. nor the methods of preparation are claimed, .apprx.150 example prepns., translations from the German examples of patent WO 9709311, are included. I inhibit β-secretase with IC50 < 50 μM; compds. that are effective inhibitors of β-secretase activity demonstrate reduced cleavage of the substrate as compared to a control. In I, R1 is aryl, heterocycle; R2 is Ph, naphthyl, acenaphthyl, cyclohexyl, pyridyl, pyrimidinyl, pyrazinyl, oxopyridinyl, diazinyl, triazolyl, thienyl, oxazolyl, oxadiazolyl, thiazolyl, **pyrrolyl**, or furyl, optionally substituted. R3 is: H, hydroxy, lower-alkoxy, or lower-alkenyloxy; R4 is: H, lower-alkyl, lower-alkenyl, lower-alkoxy, hydroxy-lower-alkyl, lower-alkoxy-lower-alkyl, benzyl, oxo, or where R3 and R4 together are a bond, or as specified in the claims. Q is: ethylene, or is absent; X is: a bond, -O-, -S-, -CH-R11- (R11 defined in claims), -CHOR9- (R9 defined in claims), -OCO, -CO-, or C:NOR10- (R10 is carboxyalkyl, alkoxycarbonylalkyl, alkyl or H), with the bond emanating from an O or S atom joining to a saturated C atom of group Z or to R1; W is: -O-, or -S-; Z is: lower-alkylene, lower-alkenylene, hydroxy-lower-alkylidene, -O-, -S-, -O-Alk- (Alk is a lower alkylene), -S-Alk-, -Alk-O-, or -Alk-S. N is: 1, or 0 or 1 when X is -O-CO; and where m is 0 or 1; with provisos.

L9 ANSWER 23 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of spirotricyclic quinoline derivatives and analogs and their use as phosphodiesterase-7 inhibitors

GI



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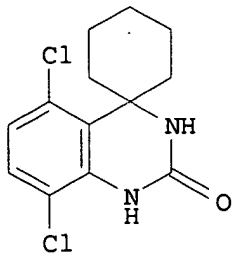


II

AB Title compds. I [X1-4 = N provided that not more than two of X1-4 simultaneously represent N; C-R1; R1 = Q1, alk(en/yn)yl, Q1 = H, halo, CN, NO2, SO3H, etc.; when X1-2 both represent C-R1, the 2 substituents R1 may form together with the carbon atoms to which they are attached, a 5-membered heterocyclic ring; X is O, NR9; R9 = H, CN, OH, NH2, alk(en/yn)yl; Y = O, S, NR12; R12 = H, CN, OH, NH2, alk(en/yn)yl; Z = CH-NO2, O, S, NR13; R13 = H, CN, OH, NH2, aryl, heteroaryl, cycloalkyl, etc,; A = cyclohexyl, heterocyclyl, etc. and tautomeric analogs] were prepared For instance, II was prepared from 2,5-dichlorophenylurea, cyclohexanone and polyphosphoric acid in 7% yield. II had IC50 = 0.014 μM for the PDE7 receptor. I are useful for the treatment of autoimmune diseases, osteoarthritis, etc.

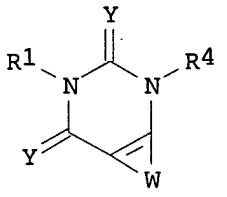
L9 ANSWER 24 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Isomerization of cyclic ethers having a carbonyl functional group: new entries into different heterocyclic compounds

AB **Oxiranes** (epoxides) and oxetanes having a carbonyl functional group are chemoselectively isomerized to different heterocyclic compds. via Lewis acid-promoted 1,6- and 1,7-intramol. nucleophilic attacks of the carbonyl oxygen on the electron-deficient carbon neighboring the oxonium oxygen: for example, cyclic imides to bicyclic acetals, esters to bicyclic ortho esters, sec-amides to 4,5-dihydrooxazole or 5,6-dihydro-4H-1,3-oxazines, and tert-amides to bicyclic acetals or azetidines. The intramol. attack of a 1,5-positioned carbonyl oxygen predominantly results

in a propagating-end isomerization polymerization On the other hand, cyclic ethers having a 1,8- or farther positioned carbonyl group undergo conventional ring-opening polymerization A THF (oxolane) ring does not open, even with a 1,6-positioned carbonyl group.

L9 ANSWER 25 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of thieno[2,3-d]pyrimidindiones as matrix metalloproteinase inhibitors for treatment of cancer, rheumatoid arthritis, and osteoarthritis
GI



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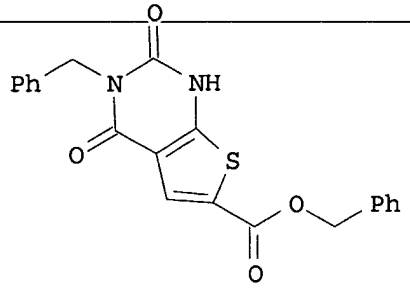
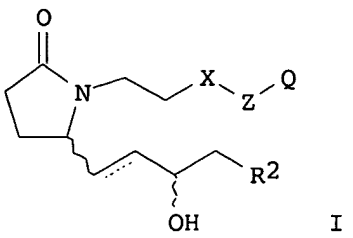


II

AB Title fused pyrimidinones I [wherein C2W = 5-membered (hetero)cyclic diradical substituted with ABR3 and optionally substituted with R2; A = CO or SO0-2; B = O or NR5; or AB = C.tplbond.C; R1, R4, and R5 = independently H, alkyl, alkenyl, alkynyl, (CH2)n-(hetero)aryl, (CH2)n-cycloalkyl, (CH2)n-heterocyclyl, or alkanoyl; R2 and R3 = independently H, alkyl, alkenyl, alkynyl CN, NO2, NR4R5, (CH2)n-cycloalkyl, or (CH2)n-(hetero)aryl; or R2 = halo; n = 0-5; or NR4R5 = (un)substituted heterocyclyl; with the proviso that R1 and R3 ≠ both H or alkyl; or pharmaceutically acceptable salts thereof] were prepared as matrix metalloproteinase (MMP) inhibitors, especially as selective MMP-13 inhibitors. For example, 3-benzyl-6-chloro-1H-pyrimidine-2,4-**dione** was coupled with mercaptoacetic acid Et ester using Na2CO3 in EtOH (67%) and the product cyclized with POCl3 in anhydrous DMF to give 3-benzyl-2,4-dioxo-1,2,3,4-tetrahydrothieno[2,3-d]pyrimidine-6-carboxylic acid Et ester (95%). Saponification (96%) followed by esterification with benzyl alc. and 1-cyclohexyl-3-(2-morpholinoethyl)carbodiimide metho-p-toluenesulfonate afforded II (12%). The latter selectively inhibited the hydrolytic activity of MMP-13 (0.61 μM) over MMP-1 (100 μM), MMP-2 (100 μM), MMP-3 (18 μM), MMP-7 (100 μM), MMP-9 (100 μM), MMP-12 (100 μM), and MMP-14 (100 μM) with the indicated IC50 values. I are useful for the treatment of diseases mediated by the MMP-13 enzyme, such as cancer, rheumatoid arthritis, or osteoarthritis (no data). Formulations of I are also disclosed.

L9 ANSWER 26 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of EP4 receptor selective agonists for the treatment of osteoporosis
GI



I

AB This invention is directed to EP4 receptor selective prostaglandin agonists I (e.g. 4-[3-[2-(3-hydroxy-4-phenylbutyl)-5-oxopyrrolidin-1-yl]propyl]benzoic acid), wherein R2, X, Z and Q are defined below and in more detail in the claims. This invention is also directed to pharmaceutical compns. containing those compds. This invention is also directed to methods of treating conditions which present with low bone mass, particularly osteoporosis, frailty, an osteoporotic fracture, a bone defect, childhood idiopathic bone loss, alveolar bone loss, mandibular bone loss, bone fracture, osteotomy, bone loss associated with periodontitis, or prosthetic ingrowth in a mammal comprising administering those compds. Although biol. testing protocols are included, no test results are given. In I, a prodrug thereof, a pharmaceutically acceptable salt of said compound or said prodrug or a stereoisomer or diastereomeric mixture of said compound, prodrug or salt: the dotted line is a bond or no bond; X is -CH2- or O; Z is -(CH2)3-, thienyl, thiazolyl or Ph, provided that when X is O, then Z is phenyl; Q is carboxy, (C1-C4)alkoxycarbonyl or tetrazolyl; R2 is -Ar or -Ar1-V-Ar2; V is a bond, -O-, -OCH2- or -CH2O-. Ar is a partially saturated, fully saturated or fully unsatd. 5-8 membered ring optionally having 1-4 heteroatoms selected independently from O, S and N, or a bicyclic ring consisting of two fused independently partially saturated, fully saturated or fully unsatd. 5-6 membered rings, taken independently, optionally having 1-4 heteroatoms selected independently from N, S and O, said partially or fully saturated ring or bicyclic ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar1 and Ar2 are each independently a partially saturated, fully saturated or fully unsatd. 5-8 membered ring optionally having 1-4 heteroatoms selected independently from O, S and N, said partially or fully saturated ring optionally having 1-2 oxo groups substituted on C or 1-2 oxo groups substituted on S. Ar is optionally substituted on C or N, on one ring if the moiety is monocyclic, or on one or both rings if the moiety is bicyclic, with up to three substituents per ring each independently selected from hydroxy, halo, carboxy, (C1-C7) alkoxy, (C1-C4)alkoxy(C1-C4)alkyl, (C1-C7)alkyl, (C2-C7)alkenyl, (C3-C7)cycloalkyl, (C3-C7)cycloalkyl(C1-C4)alkyl, (C3-C7)cycloalkyl(C1-C4)alkanoyl, formyl, (C1-C8) alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylamino, (C1-C4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylamino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N- or di-N,N-(C1-C4)alkylamino, carbamoyl, mono-N- or di-N,N-(C1-C4)alkylcarbamoyl, cyano, thiol, (C1-C6)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar are optionally substituted on C with up to three fluoro. Ar1 and Ar2 are independently optionally substituted on C or N with up to three substituents each independently selected from hydroxy, halo, carboxy, (C1-C7)alkoxy, (C1-C4)alkoxy(C1-C4)alkyl, (C1-C7)alkyl, (C2-C7)alkenyl, (C3-C7)cycloalkyl, (C3-C7)cycloalkyl(C1-C4)alkyl, (C3-C7)cycloalkyl(C1-C4)alkanoyl, formyl, (C1-C8)alkanoyl, (C1-C6)alkanoyl(C1-C6)alkyl, (C1-C4)alkanoylamino, (C1-C4)alkoxycarbonylamino, hydroxysulfonyl, aminocarbonylamino or mono-N-, di-N,N-, di-N,N'- or tri-N,N,N'-(C1-C4)alkyl substituted aminocarbonylamino, sulfonamido, (C1-C4)alkylsulfonamido, amino, mono-N- or di-N,N-(C1-C4)alkylamino, carbamoyl, mono-N- or di-N,N-(C1-

C4)alkylcarbamoyl, cyano, thiol, (C1-C6)alkylthio, (C1-C6)alkylsulfinyl, (C1-C4)alkylsulfonyl and mono-N- or di-N,N-(C1-C4)alkylaminosulfinyl, wherein said alkyl and alkoxy substituents in the definition of Ar1 and Ar2 are optionally substituted on C with up to three fluoro. (a) when X is (CH2)- and Z is -(CH2)3-, then R2 is not thienyl, Ph or Ph monosubstituted with chloro, fluoro, Ph, methoxy, trifluoromethyl or (C1-C4) alkyl; and (b) when X is (CH2)-, Z is -(CH2)3-, and Q is carboxy or (C1-C4) alkoxycarbonyl, then R2 is not (i) (C5-C7)cycloalkyl or (ii)phenyl, thienyl or furyl each of which may be optionally monosubstituted or disubstituted by one or two substituents selected, independently in the latter case, from halogen atoms, alkyl groups having 1-3 C atoms which may be substituted by one or more halogen atoms, and alkoxy groups having 1-4 C atoms. Although the methods of preparation are not claimed, 41 example prepns. are included.

L9 ANSWER 27 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI New aryl-, quinolyl-, and other heterocyclyl-containing amino alcohol derivatives useful as β3 adrenergic receptor agonists

GI

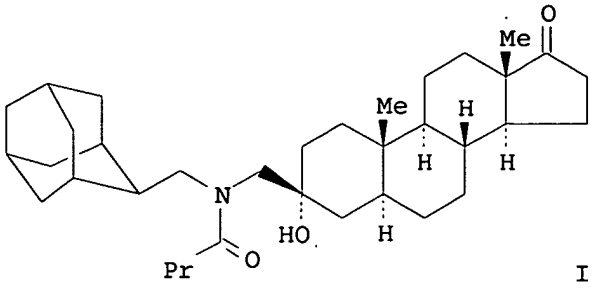
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to compds. I [wherein: X1 = bond or OCH2; X2 = (CH2)1-2; X3 = bond, O, or NH; R1 = (un)substituted Ph, indolyl, or carbazolyl [substituents = 1 or 2 of OH, halo, NO2, amino, formyl, (lower)alkylsulfonylamino, aryl(lower)alkoxy, and hydroxy(lower)alkyl]; R2 = H or aryl(lower)alkyl; R3 = H or hydroxy(lower)alkyl; R4 = (un)substituted aryl, 4-quinolyl, phthalazinyl, quinazolinyl, cinnolinyl, or naphthyridinyl; with provisos], or their pharmaceutically acceptable salts. The compds. are β3 adrenergic receptor agonists, and therefore have gut sympathomimetic, antiulcer, anti-pancreatitis, lipolytic, and smooth muscle relaxant activities. In particular, I and salts are useful for the prophylactic and/or the therapeutic treatment of pollakiuria or urinary incontinence. Sixty precursor prepns. and 63 invention examples, including well over 200 invention compds., are provided. For example, the structure of claimed compound II is typical. Another invention compound, phthalazine derivative III, was prepared from 4-((2S)-2-amino-3-hydroxypropyl)phenol HCl, benzaldehyde, (2S)-3-phenoxy-1,2-epoxypropane, and 1-chlorophthalazine, in 4 steps. III at 0.32 mg/kg (intraduodenal) in beagle dogs gave 35.9% inhibition of carbachol-induced increase in intravesical pressure.

L9 ANSWER 28 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Synthesis and Optimization of a New Family of Type 3 17β-Hydroxysteroid Dehydrogenase Inhibitors by Parallel Liquid-Phase Chemistry

GI



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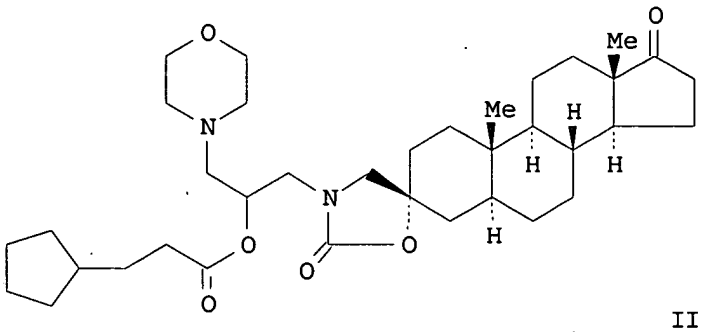

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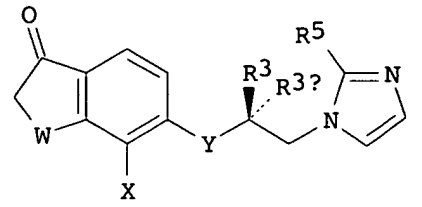
AB Type 3 17β-hydroxysteroid dehydrogenase (17β-HSD) transforms 4-androstene-3,17-**dione** (Δ4- **dione**) into the androgen testosterone. To produce potent inhibitors of this key steroidogenic enzyme, we performed parallel liquid-phase synthesis of 3β-substituted androsterone (ADT) libraries (A-D) in good yields and average high-performance liquid chromatog. (HPLC) purities of 92-94%. The first library (A) of 3β-amidomethyl-ADT derivs. (168 members), including two levels of mol. diversity on the amide (R1 and R2), was synthesized with a parallel liquid-phase method (method I) in less time than with the classic chemical method. The screening of library A revealed that relatively small hydrophobic chains at R1 (5-8 carbons) and small hydrophobic substituents at R2 (1-4 carbons) provided the most potent inhibitors. In accordance with these inhibition results, a second library (B) of 3β-amidomethyl-ADT derivs. (56 members) was generated in a very short time using an improved method based on scavenger resins and liquid-phase parallel chemical Library B produced more potent inhibitors than library A and provided useful structure-activity relationships that directed the design of a third library (C) of 49 members. Once again, very potent inhibitors were identified from library C and 3β-[(N-adamantylmethyl-N-butanoyl)aminomethyl]-3α-hydroxy-5α-androstan-17-one (I) was identified as the most potent inhibitor of the three libraries with an inhibitory activity (IC50 = 35 nM) 18-fold higher than that of the natural substrate of the enzyme, Δ4- **dione**, (IC50 = 650 nM) used itself as inhibitor. Finally, we designed a library (D) of 3-carbamate-ADT derivs. (25 members) using the efficient parallel liquid-phase method III, which allowed the synthesis of more rigid mols. with two levels of mol. diversity (R1/R2 and R3) in the local area occupied by the adamantane group of I. Interestingly, one of the most potent inhibitors of library D, the 3R-spiro-[3'-[3''-N-morpholino-2''-(3'''-cyclopentylpropionyloxy)propyl]-2'-oxooxazolidin-5'-yl]-5α-androstan-17-one (II), showed an inhibitory activity on type 3 17β-HSD similar to that of compound I, while exhibiting a nonandrogenic profile.

L9 ANSWER 29 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of 5-substituted tetralones as inhibitors of ras farnesyl transferase for treatment of proliferative diseases

GI



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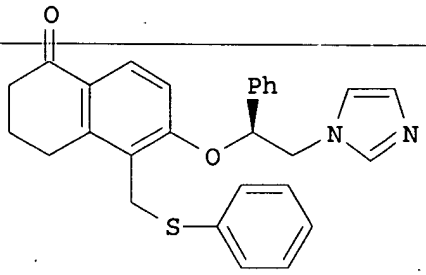


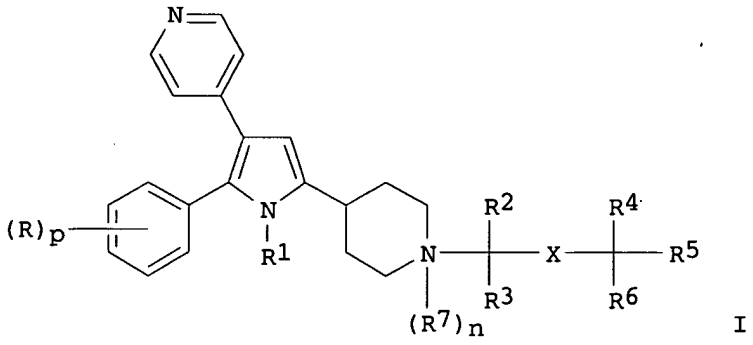
II

AB Title compds. I [wherein W = CH2 or CH2CH2; R3 = H, alkyl, or (un)substituted Ph; R3a = H or alkyl; provided that R3 and R3a cannot both be H and that when R3 = (un)substituted Ph, then R3a = H; X = halo, NH2, alkyl, alkenyl, heteroaryl, CH2OR6, CH2NR6R6a, CH2SR6, CH2CH2CO2R6, or (un)substituted aryl, or (hetero)arylalkyl; R6 = H, (cyclo)alkyl, alkenyl, benzyl, or (un)substituted Ph; R6a = H or alkyl; Y = O or S; R5 = H, alkyl, or NH2; and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof] were prepared and formulated as farnesyl transferase enzyme inhibitors. For example, coupling of 5-chloromethyl-6-hydroxy-2,3,4-trihydronaphthalen-1-one with thiophenol using diisopropylamine in THF (58%), followed by addition of (R)-2-imidazol-1-yl-1-phenylethanol in the presence of PPh3 and di-Et azodicarboxylate in THF (31%), gave II. The latter inhibited farnesyl protein transferase (FPT) with IC50 of 0.3 nM. I are useful for treating and preventing uncontrolled or abnormal proliferation of tissues, such as cancer, atherosclerosis, restenosis, and psoriasis (no data).

L9 ANSWER 30 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Aliphatic hydroxy substituted piperidyl diaryl **pyrrole** derivatives as antiprotozoal agents

GI



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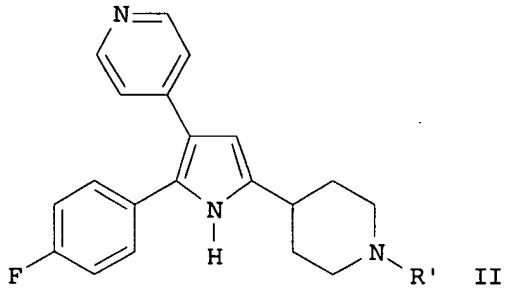
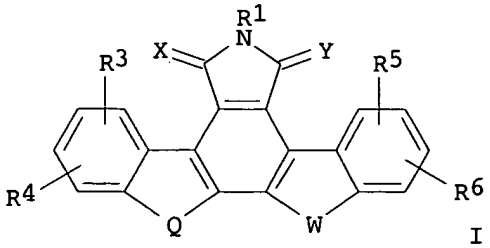


II

AB Trisubstituted **pyrroles** I are antiprotozoal agents (no data), useful in the treatment and prevention of protozoal diseases in human and animals, including the control of coccidiosis in poultry [wherein: n = 0-1; p = 1-3; X = bond, (un)substituted (CH2)1-3, cycloalkylene, cycloalkylidene; R = halo; R1 = H or alkyl; R2, R3 = H, (un)substituted alkyl, alkenyl, alkynyl, (un)substituted Ph or CH2Ph, CO2H or derivs.; or R2R3 = O; R4 = OH or SH or their derivs.; R5, R6 = H, alk(en/yn)yl, cycloalkyl(alkyl), (hetero)aryl(alkyl), heterocyclyl(alkyl), CO2H or OH or derivs.; or R4R5 or R5R6 forms 3- to 7-membered hetero ring; or R4R6 = O; or R2R4 or R2R5 forms 4- to 7-membered carbo or hetero ring; R7 = O, Me; and physiol. acceptable salts]. Approx. 200 compds. were prepared For instance, 4-picoline was lithiated and condensed with 4-FC6H4CONMeOMe, and the resulting ketone was deprotonated and coupled with 4-(2-iodoacetyl)-1-(benzyloxycarbonyl)piperidine to give a 1,4-diketone. Cyclization of this with ammonium acetate and deprotection gave **pyrrole** intermediate II [R' = H], which was N-alkylated by (R)-glycidyl Me ether to give title compound II [R' = (R)-CH2CH(OH)CH2OMe].

L9 ANSWER 31 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Synthesis and pharmacological studies of 1-p-nitrobenzoyl-3-(3-substituted-2-hydroxypropyloximino) indole-2,3-**diones**
AB The sodium salt of indole-2,3-**dione** 3-oxime (prepared in situ) with epichlorohydrin in DMF gave 3-[(**oxiranylmethoxy**)imino]-1H-indol-2-one. On reaction with secondary amines, this compound gave the corresponding Mannich bases, which on benzoylation furnish the title compds., i.e., 3-[(3-amino-2-hydroxypropoxy)imino]-1-(4-nitrobenzoyl)-1H-indol-2-one derivs. Some synthetic benzoyl derivs. were screened for their pharmacol. activities.

L9 ANSWER 32 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of cyclic substituted fused **pyrrolocarbazoles** and isoindolones with protein kinase inhibiting activity for pharmaceutical use
GI



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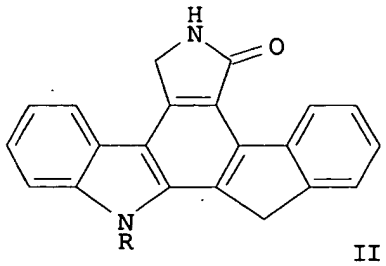
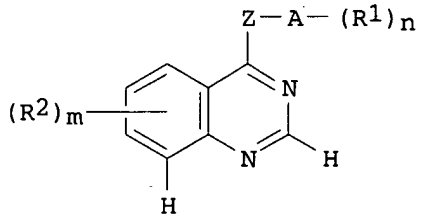


II

AB Fused **pyrrolocarbazoles** and isoindolones, such as I [R1 = H, alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl; R3-6 = H, CN, CF3, OH, CH2OH, halogen, aryl, heteroaryl, acyl, acyloxy, amino, etc.; Q = O, S, NR7; W = CR8R9; X, Y = H2, O; R7 = H, alkyl, heterocyclylalkyl, etc.; R8, R9 = H, OH, cycloalkyl, cycloalkylmethyl, heterocyclyl, heterocyclylalkyl, etc.], were prepared for use as agents for the regulation of protein kinase and for the treatment of prostate disorders, neoplasia, rheumatoid arthritis, pulmonary fibrosis, etc. Thus, II (R = **oxiranylmethyl**) was prepared in 71% yield by via reaction of (±)-glycidyl mesylate and Rink's acid resin bound 6,7,12,13-tetrahydro-5H-indeno[2,1-a]**pyrrolo**[3,4-c]carbazol-5-one. The prepared compds. were tested for inhibitory activity against a variety of protein kinases, such as trkA tyrosine kinase, vascular endothelial growth factor receptor kinase, protein kinase C, etc.

L9 ANSWER 33 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of quinazoline derivatives as angiogenesis inhibitors
GI



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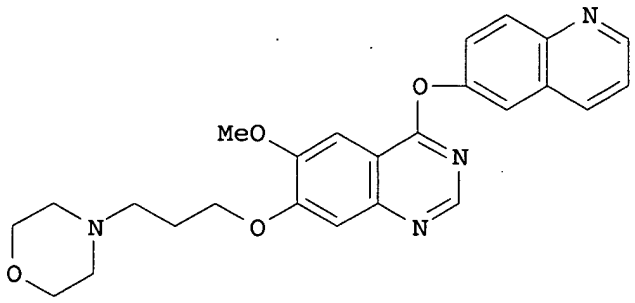


II

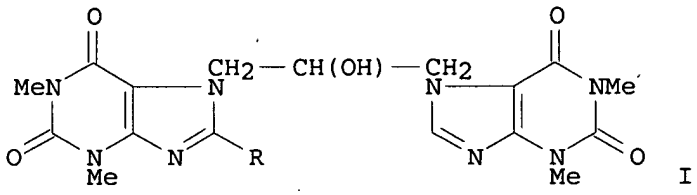
AB The title compds. (I) [wherein A = an 8-, 9-, 10-, 12- or 13-membered bicyclic or tricyclic ring optionally containing 1-3 O, N, and/or S heteroatoms; Z = O, NH, S, CH2, or a bond; n = 0-5; m = 0-3; R2 = H, OH, halo, CN, NO2, CF3, alkyl(sulfanyl), alkoxy, NR3N4, or R5X1; R3 and R4 = independently H or alkyl; X1 = a bond, O, CH2, OC(O), CO, S, SO, SO2, NR6CO, CONR7, SO2R8, NR9SO2, or NR10; R5 = H or (un)substituted alkyl, alkenyl, alkynyl, or heterocyclyl, etc.; R6-R10 = independently H or

(alkoxy)alkyl] were prepared for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals. For instance, II was synthesized in a 9-step sequence starting with the cyclization of 2-amino-4-benzyloxy-5-methoxybenzamide using Gold's reagent in dioxane to form 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one (84%). I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis (no data).

L9 ANSWER 34 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Concentration of organic pollutants in water by supercritical fluid extraction
AB A combined method of solid phase adsorption and supercrit. fluid extraction (SFE) has been used for collecting and concentrating organic pollutants from sewage for determination by GCMS. Eight factors were studied for the optimization of SFE conditions. The extraction efficiencies for the test compds. were over 70%, and the relative standard deviation was <4.6% (n = 3). In this manner, 66 organic pollutants were detected in the sewage. Among them, 15 appeared in the list of priority pollutant suggested by US EPA. Benzothiazole, amines and phenols were the predominant organic pollutants. The contents of the contaminants in the wastewater before and after treatment were compared.

L9 ANSWER 35 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Calculation of retention indexes of low-boiling organic compounds of different chemical nature on the polymer sorbent Porapak Q
AB The procedures that have been developed previously for the calcns. of chromatog. retention indexes from the physicochem. consts. of organic compds. can be extended to compds. of any chemical nature. Using the retention indexes of low-boiling compds. R-X (X is variable fragments of mol. composition or structure) on the polymeric sorbent Porapak Q as examples, these indexes can be calculated from data on the boiling temps. under atmospheric pressure and from the increments of the atomic or group refractions of X fragments.

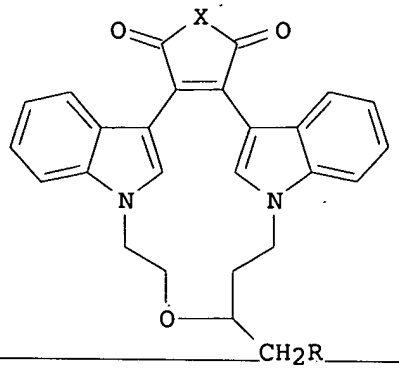
L9 ANSWER 36 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Studies on the methylxanthine series. IX. Synthesis and physicochemical characterization of 1-(8-substituted 1,3-dimethylxanthin-7-yl)-3-(1,3-dimethylxanthin-7-yl)-2-hydroxypropane derivatives
GI



I

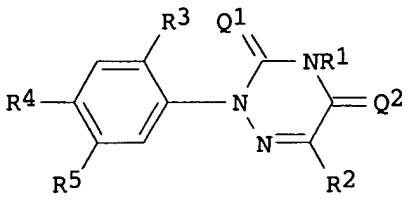
AB Title compds. I (R = H, Br, NO2, 1-**pyrrolidinyl**, piperidino, morpholino, etc.) were prepared by reaction of 8-substituted 1,3-dimethylxanthines with 7-(epoxypropyl)-1,3-dimethylxanthine.

L9 ANSWER 37 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of bis-indolylmaleimide macrocycle derivative as protein kinase C inhibitor
GI



AB This invention provides novel bis-indolylmaleimide macrocycle derivs. of the formula (I.MeSO3H; X = NH, R = NMe2) and solvates thereof, in particular (S)-I.MeSO3H (X = NH, R = NMe2), namely (S)-13-[(dimethylamino) methyl]-10,11,14,15-tetrahydro-4,9:16,21-dimetheno-1H, 13H-dibenzo[E,K] **pyrrolo**[3,4-H][1,4,13]-oxadiazacyclohexadecine-1,3(2H)-**dione** methanesulfonate monohydrate. The invention further provides the preparation, pharmaceutical formulations and the methods of use for inhibiting protein kinase c in mammals. A method of treating microvascular diabetic complications comprises administering to a mammal in need thereof, a pharmaceutically effective amount of a compound of I.MeSO3H (X = NH, R = NMe). Most unexpectedly, the claimed mesylate salt form has improved solubility and dramatically improved bioavailability to the patient and furthermore, is readily prepared and purified as a crystalline form. Thereby, it is more pharmaceutically elegant and a much improved therapeutic agent and is useful in treating conditions associated with diabetes mellitus and its complications, ischemia, inflammation, central nervous system disorders, cardiovascular disease, dermatol. disease, and cancer (no data). Thus, 2,3-bis(1H-indol-3-yl)-N-methylmaleimide was cyclocondensed with (S)-3-[2-(methanesulfonyloxy)ethoxy]-4-trityloxy-1-(methanesulfonyloxy)butane methanesulfonate in the presence of Cesium carbonate in DMF at 50° for 70-72 h to give 89% (S)-I (X = NMe, R = OCPh3) which was suspended in EtOH and 10 N aqueous KOH, heated to a gentle reflux, and acidified with aqueous 10N HCl to give 80% (S)-I (X = O, R = OCPh3). The latter compound was dissolved in DMF, treated with a premixed solution of MeOH and 1,1,1,3,3,3-hexamethyldisilazane, and heated at 45° for 7 h to give 100% (S)-I (X = NH, R = OCPh3), which was detritylated with HCl in CH2Cl2 to give 90% (S)-I (X = NH, R = OH) and then mesylated by methanesulfonic anhydride in pyridine and THF to give 81% (S)-I (X = NH, R = OSO2Me). This was heated with a mixture of 40% aqueous Me2NH and THF at 65° in a sealed reactor for 19 h to give 91% (S)-I (X = NH, R = NMe2), which was converted into the mesylate salt (S)-I.MeSO3H (X = NH, R = NMe2). The solubility of the mesylate salt in water was 1,760 μg/mL compared to 0.5, 1, 14, 71, 268, and 736 μg/mL for the succinate, acetate, sulfate, hydrochloride, and phosphate salt of (S)-I (X = NH, R = NMe2). It showed greater than 1.5 times the bioavailability of the HCl salt when administered p.o. to dogs. Formulations such as hard gelatin capsules, tablet, and capsules containing I.MeSO3H were described.

L9 ANSWER 38 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of 2-aryl-1,2,4-triazine-3,5-di(thi)ones as herbicides
GI



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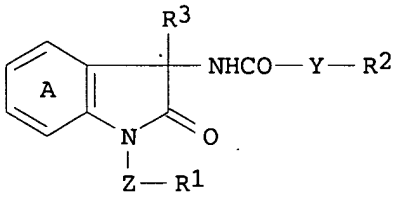
AB Title compds. [I; Q1, Q2 = O, S; R1 = H, cyano, amino, (substituted) alkyl, alkoxy, alkylamino, dialkylamino, alkylcarbonyl alkoxycarbonyl, alkenyl, alkenylcarbonyl, alkenyloxycarbonyl, alkynyl, alkynylcarbonyl, alkynyloxycarbonyl, cycloalkyl, cycloalkylalkyl; R2 = H, halo, NO2, CO2H, cyano, thiocarbamoyl, amino, (substituted) alkyl, alkoxy, alkylthio, alkylamino, dialkylamino, alkenyl, alkenyloxy, alkenylthio, alkynyl, alkynyloxy, alkynylthio, cycloalkyl, cycloalkylalkyl; R3 = halo; R4 = cyano, thiocarbamoyl; R5 = A1A2A3; A1, A2 = bond, O, S, SO, SO2, CO, NA4, (halo-substituted) alkylene, alkenylene, etc.; A4 = H, OH, alkyl, alkenyl, alkynyl, alkoxy, aryl, alkylcarbonyl, alkylsulfonyl, arylsulfonyl, arylcarbonyl; A3 = H, OH, SH, amino, cyano, isocyano, thiocyanato, NO2, CO2H, carbamoyl, thiocarbamoyl, sulfo, halo, (substituted) alkyl, alkoxy, alkylthio, alkylsulfinyl, (partially or fully reduced) **pyrrolyl**, pyrazolyl, imidazolyl, triazolyl, furyl, **oxiranyl**, oxetanyl, dioxolanyl, thienyl, oxazolyl, etc.], were prepared Thus, 4-amino-6-methyl-1,2,4-triazin-3,5(2H,4H)-**dione**, 2,4,5-trifluorobenzonitrile, and K2CO3 were stirred at 70° in Me2SO to give 20% 2-(2,4-difluoro-4-cyanophenyl)-4-amino-4-methyl-1,2,4-triazin-3,5(2H,4H)-**dione.** Several I at 60-125 g/ha gave 100% control of Amaranthus, Chenopodium, and Solanum.

L9 ANSWER 39 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of 2-oxoindoline derivatives as cholecystokinin antagonists
GI



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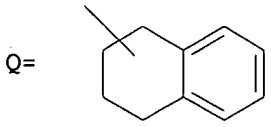

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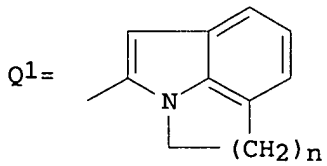

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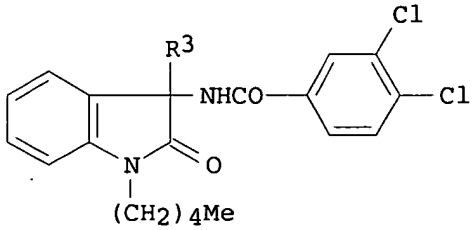


II

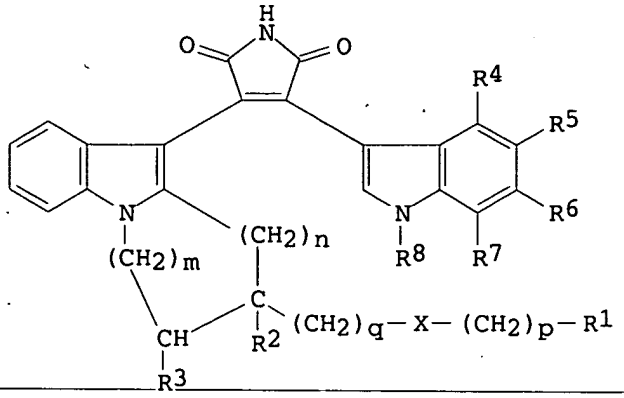
AB The title compds. [I; ring A represents (un)substituted benzene; R1 = H, cycloalkyl, aryl, nitrogen heterocycle, oxygen heterocycle, sulfur heterocycle, heterocycle containing N and O, heterocycle containing N and S, lower alkoxy, CO2H, cyano, lower alkylthio, lower alkylsulfinyl, lower alkylsulfonyl, **oxiranyl**, or 2-(lower alkylthio)-1-hydroxyethyl; R2 = aryl, Q, (un)substituted nitrogenous monocyclic heterocyclyl, (un)substituted nitrogenous bicyclic heterocyclyl, Q1 (wherein n = 1, 2),

oxygen heterocyclyl, sulfur heterocyclyl, heterocyclyl containing N and O, heterocyclyl containing N and S; R3 = (un)substituted lower alkyl; Z = a single bond or lower alkylene; Y = a single bond, lower alkylene or alkenylene], useful for the treatment of pancreas disorders such as acute and chronic pancreatitis and pancreas cancer, diseases of stomach and intestines such as irritable bowel syndrome, reflux esophagitis non-ulcer dyspepsia, and biliary colics (no data), are prepared Thus, 2.84 g 3-amino-1-pentyl-2,3-dihydro-1H-indol-2-one hydrochloride was condensed with 2.80 g 3,4-dichlorobenzoyl chloride in the presence of NaHCO3 in H2O/CHCl3 under ice-cooling for 30 min and at room temperature for 30 min to give 4.06 g intermediate (II; R3 = H). The latter compound (3.56 g) was stirred overnight with 4.1 mL Me acrylate in the presence of K2CO3 in acetone to give 3.96 g title compound II (R3 = CH2CH2CO2Me). A total of 184 I were prepared

L9 ANSWER 40 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI MAB, a generally applicable molecular force field for structure modeling in medicinal chemistry
AB The math. formulation, parametrization scheme, and structural results of a new, generally applicable mol. force field are presented. The central features are a scheme for automatic parameter assignments, the consistent united-atom approximation, the absence of atom types other than elements, the replacement of electrostatic terms by geometrical hydrogen-bonding terms, the concomitant lack of a need for partial atomic charge assignment and the strict adherence to a finite-range design. As a consequence of omitting all hydrogen atoms, optimal hydrogen-bond patterns are computed dynamically by appropriate network analyses. For a test set of 1589 structures, selected from the Cambridge Structural Database solely on the grounds of a given element list and criteria for high structure refinement, the agreements are on average 2 pm for bonds, 2° for valence angles and 10 to 20 pm for the root-mean-square deviation of atom positions, depending somewhat on size and flexibility of the structures. More qual. testing of large-scale structural properties of the force field on proteins and DNA oligomers revealed satisfactory performance.

L9 ANSWER 41 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Detection and identification of volatile substances by headspace capillary gas chromatography to aid the diagnosis of acute poisoning
AB Headspace gas chromatog. with split flame-ionization-electron-capture detection is a simple method of screening for a wide range of volatile substances in biol. fluids. A 60 m x 0.53 mm i.d. thick-film (5 μm) fused-silica capillary coated with SPB-1 (Supelchem) with split flame-ionization-electron-capture detection provides a valuable alternative to packed columns in this work. Most commonly abused compds., including many with very low b.ps. such as bromochlorodifluoromethane, butane, di-Me ether, FC 11, FC 12, isobutane, and propane, can be retained and differentiated at an initial column temperature of 40° followed by programming to 200°. The total anal. time is 26 min. Retention and detector response date were generated for 244 compds. Good peak shapes are obtained for polar analytes such as ethanol and injections of up to 0.03 cm3 of headspace can be performed with no discernable loss of efficiency. The sensitivity is thus at least as good as that attainable with packed columns. Of the commonly encountered compds., only isobutane-methanol and paraldehyde-toluene are at all difficult to differentiate. Quant. measurements can be performed either isothermally or by using the temperature program.

L9 ANSWER 42 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of 3-pyridopyrroloindolyl-4-indolylpyrrole-2,5-**diones** as protein kinase inhibitors
GI



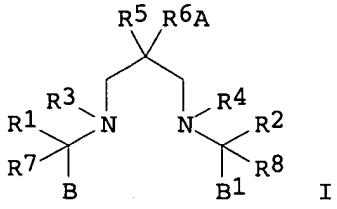
I

AB The title compds. [I; R1R3 = bond, R2 = H or R1R2 = bond, R3 = H; R4-R7 = H, halo, (halo)alkyl, alkoxy, NO2, (alkanoyl)amino, alkylthio, alkylsulfonyl; R8 = H, alkyl, aralkyl; X = NR9, CHNR10R11; R9-R11 = H, alkyl, aralkyl, alkanoyl; m = 0-2; n = 1-3; m + n = 1-3; p, q = 0-4, with provisos] and their pharmaceutically acceptable salts, useful for the control or prevention of, e.g., arthritis, psoriasis, AIDS, asthma, thrombosis, etc., were prepared by reaction of the appropriate furandione analogs (also claimed) with NH(SiMe3)2 or aqueous NH3 under pressure. Thus, trans-2-(tert-butoxycarbonyl)-2,3,3a,4,11,11a-hexahydro-1H-**pyrrolo**[3',4':4,5]pyrido[1,2-a]indole (multistep preparation from di-Et 6,7-dihydro-9-hydroxypyrido[1,2-a]indole-7,8-dicarboxylate given) was condensed with (COCl)2, the dicarbonyl chloride derivative cyclocondensed with 1-methylindole-3-acetic acid, and the resulting furan-2,5-**dione** converted to its HCl salt. This was methylated by aqueous HCHO in the presence of Raney Ni, neutralized by HCl, and stirred with NH(SiMe3)2 in DMF/MeOH to give title product trans-3-(2,3,3a,4,11,11a-hexahydro-2-methyl-1H-**pyrrolo**[3',4':4,5]pyrido[1,2-a]indol-10-yl)-4-(1-methyl-3-indolyl)-1H-**pyrrole**-2,5-**dione** which was converted to its HCl salt. The latter in vitro (test form unspecified) inhibited protein kinase with IC50 of 7 nM.

L9 ANSWER 43 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of propanediamine derivatives as ligands for radioactive isotopes, their metal complexes, and their use in diagnosis and therapy

GI



I

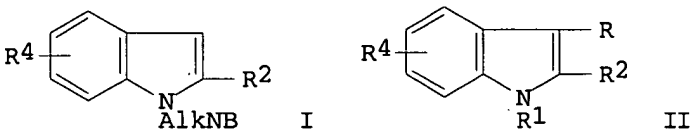
AB The title ligands [I; R1, R2, R5 = H, (HO-substituted) C1-6 alkyl; R3, R4 = H, (amino)C1-6 alkyl, HO2CCH2, (C1-6 alkoxycarbonyl)methyl or -benzyl; R6 = C1-6 alkylene; R7, R8 = H, C1-6 alkyl; B, B1 = Ph, 2-HSC6H4, naphthyl, thienyl, **pyrrolyl**, all optionally substituted by 1-3 HO), CH(NO)R9; R9 = C1-6 alkyl; R1R9, R2R9 can form a 5- or 6-membered ring with (CH2)3 or (CH2)4; A = functional group Z, a compound T bound to R6 via Z and capable of accumulating itself in lesions or specific tissues, e.g. an enzyme, amino acid, saccharide, a growth factor, especially a monoclonal antibody or its fragments, biotin, and misonidazole; Z = amino, carboxy,

HO, **oxiranyl**, aminophenyl, C2-6 alkenyl, etc.], useful in tumor diagnosis and therapy, were prepared Condensation of 4-O2NC6H4CH(CH2NH2)2 [preparation from CH2(CO2Et)2 and 4-O2NC6H4CH2Br given] with 2-chloro-2-methyl-3-nitrosobutane gave 27% 6-(4'-nitrobenzyl)-3,3,9,9-tetramethyl-4,8-diazaundecane-2,10-**dione** dioxime. This was reduced (26%) to its 4'-aminobenzyl analog, chelated by Cu(OAc)2 (45%), the Cu-chelate coupled (75%) at position 4' with biotin N-hydroxysuccinimide ester, the resulting biotin conjugate decomplexed (41%) by KCN, and the ligand recomplexed with a radioactive tracer: technetium-99m (200 μCi). A rat left hind leg muscle was injected with 20 μL of a com. streptavidin-Sepharose conjugate and, 30 min later, with 5 μg (i.v.) of the latter chelate (purity >90%). After 4 h, the radioactivity in the left hind leg was 14-fold higher than in the right hind leg, and it contained 1.4% of the total of the applied dosis/g muscle.

L9 ANSWER 44 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Preparation of 1-(aminoalkyl)indoles useful as analgesic agents or as intermediates and their production processes

GI



AB Title compds. I [R2 = H, alkyl, Cl, (un)substituted Ph, (un)substituted PhCH2; R4 = H, 1 or 2 substituents such as alkyl, HO, alkoxy, halo in 4-, 5-, 6-, or 7 position; alk = (un)substituted α,ω-alkylene (CH2)n; n = 2-6; NB = N3, H2N, alkylamino, hydroxyalkylamino, morpholino, thiomorpholino, piperidino, **pyrrolidino**, azetidino, **pyrrolidino**, 1-piperazinyl, hexahydro-4H-1,4-diazepinyl, their oxides, etc.] or an acid addition salt thereof, useful as analgesics (no data) are prepared II (R = R3CZ, R3COCH:CH, R3CO; R3 = cyclohexyl, heterocycylphenyl, aminomethylphenyl, (un)substituted styryl, biphenyl, (un)substituted naphthyl, heterocyclyl, etc.; CZ = CO, HONC; R1 = H, BNAlk, BNCH2CH(OH)CH2] were also prepared and found to possess analgesic, antiinflammatory and antirheumatic activities. II [R = 3-(O2N)C6H4CO; R1 = 2-morpholinoethyl; R2 = Me; R4 = H] in EtOAc and AcOH was reduced with H over Pt oxide to give 83% II [R = 3-(H2N)C6H4CO; R4 = morphoninoethyl; R2 = Me; R4 = H] (III). III, on oral administration, showed and ED50 in acetylcholine-induced abdominal constriction and antibradykinin test of 16 and 53 mg, resp., and on the rat paw flexion test 0.12% at 100 mg/kg.

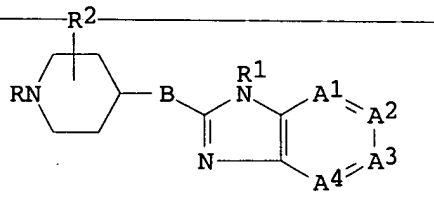
L9 ANSWER 45 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI The structural basis of the mutagenicity of chemicals in Salmonella typhimurium: The Gene-Tox data base

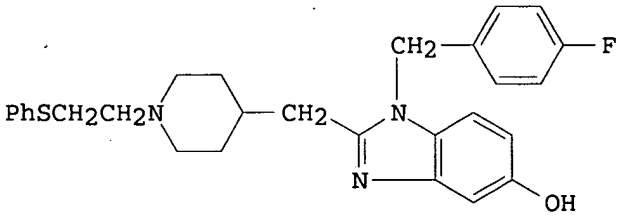
AB The CASE (Computer Automated Structure Evaluation) structure-activity methodol. has been applied to a Gene-Tox derived Salmonella mutagenicity data base consisting of 808 chems. Based upon qual. structural features, CASE identified 29 activating and 3 inactivating structural determinants which correctly predicted the probability of carcinogenicity of 93.7% of the known mutagens and nonmutagens in the data base (sensitivity = 0.998, and specificity = 0.704). Addnl., based upon a qual. structure-activity anal., CASE's performance was even better, leading to a sensitivity of 0.981 and a specificity of 1.000. Using the structural determinants identified in this data base, CASE gave excellent predictions of the mutagenicity of chems. not included in the data base. The identified biophores and biophobes can also be used to investigate the structural basis of the mutagenicity of various chemical classes.

L9 ANSWER 46 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI A new method for the estimation of partition coefficient [Erratum to document cited in CA110(25):231045Z]
AB An error in equation 10 has been corrected The error was not reflected in the abstract or the index entries.

L9 ANSWER 47 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of 4-[(bicyclic heterocyclyl)methyl]piperidines and analogs as antihistaminics
GI



I



II

AB The title compds. [I; 3 of A1-A4 = (un)substituted CH, the 4th = N, (un)substituted CH; B = CH2, O, SO, SO2; R = substituted C1-6 alkyl, alkoxy, alkylthio, amino, **pyrrolidinyl**, piperidinyl, hexahydroazepinyl, etc.; R1 = H, alkyl, cycloalkyl, (un)substituted aryl, heteroaryl, (hetero)aralkyl; R2 = H, alkyl] and their stereoisomers and acid salts were prepared as antihistaminics and serotonin antagonists. 1-[(4-Fluorophenyl)methyl]-2-(4-piperidinylmethyl)-1H-benzimidazol-5-ol and PhSCH2CH2Br were refluxed 2 h in Me2CHCH2COMe containing Na2CO3 to give 27.8% benzimidazole derivative (II). I inhibited compound 48/80-induced lethality in rats, caused by histamine release, with ED50 of 0.005-0.16 mg/kg s.c. or orally. I also inhibited gastric lesions caused by simultaneous release of serotonin.

L9 ANSWER 48 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Substituted hexahydroarenoquinolizines and their use
GI For diagram(s), see printed CA Issue.
AB The title compds. [I; Ar = fused (hetero)areno selected from (un)substituted benzo[b]furo, benzo[b]thieno, pyridino, thieno, thiazolo, imidazo, pyrazolo; B = 4-7 membered spiroheterocycle residue; R = H, (un)substituted OH, NHCHO, NHCOR1 (R1 = alkyl), or CO2H], selective α2-adrenergic receptor antagonists and thereby useful as antidepressants, antihypertensives, ocular antihypertensives, antidiabetics, platelet aggregation inhibitors, and antiobesity agents (no data), were prepared Thus, 10-methyl-1,3,4,6,7,12b-hexahydrobenzo[b]thieno[2,3-a]quinolizin-2-one and (EtO)2P(O)CN were added to a saturated solution of MeNH2 in dry THF at 0° under ice-cooling and the mixture was allowed to react at 0°-room temperature over night to give 2-cyano-2-(methylamino)-10-methyl-1,3,4,6,7,12b-hexahydrobenzo[b]thieno[2,3-a]quinolizine. Borane reduction of this in THF and reaction of the resulting diamine with carbonyldiimidazole in CHCl3 gave spiro[benzothienoquinolizine-2,4'-imidazolidine] derivative II.

L9 ANSWER 49 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Heat-resistant compositions for bearings
AB The reaction products of N,N'-methylenebis(phenylmaleimide) [13676-54-5] or N,N'-oxybis(phenylmaleimide) (I) [13132-94-0] with isocyanuric acid (II) [504-19-8] derivs. were used to prepare heat-resistant compns. Thus, 0.5 mole I and 0.1 mole Bu glycidyl ether [2426-08-6]-modified II were heated in 250 g DMF at 150-5°, mixed (206 parts resin) with 200 parts powdered graphite and 20 parts graphite fibers, added to 4 l. water, filtered, washed, dried, molded at 200° (100-300 kg/cm2), and hardened at 225° for 15 hr to prepare a sheet having low friction.

L9 ANSWER 50 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Arylimide-epoxy resin composites
GI For diagram(s), see printed CA Issue.
AB Resin compns. suitable for curing to tough thermally stable thermoset composites having high glass transition temps., Tg and high modulus plateaus above Tg contain 5-95% arylimide (I; q = 6-8; s = 1-2) (prepared from chlorinated terphenyl-sodium aminophenolate polyamines and maleic anhydride) and 95-5% epoxy resin. Thus, 11.05 lb 49.7% NaOH was added to a refluxing mixture containing 15.14 lb p-aminophenol [123-30-8], 38.19 lb Aroclor 5460 [11126-42-4], 8.0 gal xylene, and 9.0 gal N-methylpyrrolidinone, xylene was distilled until pot temperature 165° was attained, and 13.61 g maleic anhydride [108-31-6] was added. A mixture of 70 g arylimide product and 30 g epoxylated novolak with epoxy equivalent 180-220 g/g-mole **oxirane** oxygen was melt blended at 160°, B-staged for 2 min at 265°, and compression molded for 3 min at 265°. The thermoset composite had Tg 35,000 psi, shear modulus 1.1 + 1010 dynes/cm2, and shear modulus above Tg 8.5 + 108 dynes/cm2.

L9 ANSWER 51 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Resin laminates
AB Substrates were coated with mixts. of bismaleimides 30-60, epoxy compds. 65-25, and cyanuric acid [108-80-5] 5-15% and laminated by heating under pressure. Thus, Epikote 1007 [25068-38-6] 19, an alkyl-modified bisphenol epoxy resin 35, and isocyanuric acid [108-80-5] 11 parts were dissolved in DMF to give a 50% solution, stirred at 150-5° for .apprx.3 hr, mixed with 35 parts N,N'-(methylenedi-p-phenylene)bismaleimide [13676-54-5], diluted with DMF to 50%, coated on glass cloths treated with γ-aminopropyltriethoxysilane, and dried at 160° for 5 min to prepare prepregs which were pressed at 180° (50 kg/cm2) to form a laminate.

L9 ANSWER 52 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Heat-hardenable compositions
AB Reaction of epoxy resins with bis(4-aminophenyl)methane [101-77-9] and 4-maleimido-4'-acetamidodiphenylmethane [53184-84-2], 4,4'-diphenylmethanebismaleimide [13676-54-5] or 4-maleimido-4'-acetoxysuccinimidodiphenylmethane [53184-85-3] gave heat hardenable moldings.

L9 ANSWER 53 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of water-soluble copolymers from ethylene oxide and epichlorohydrin
AB Epichlorohydrin-ethylene oxide copolymer (I) [24969-10-6] was prepared in the presence of Et3Al-H2O catalyst system containing various electron-donating additives, and converted into derivs. containing amino or imino groups in the side-chains by treatment with metal salts of amines or imines. Highest yields and highest viscosities of I were obtained with systems containing dimethyl ether [115-10-6], diethyl ether [60-29-7], THF [109-99-9], diethylaniline [91-66-7], or anisole [100-66-3]. Treatment of I with Na amide [7782-92-5], Na acetamide [2620-30-6], silver imidazole [42879-93-6], etc., yielded the corresponding derivs. with .leq. 100% substitution degree. I underwent partial degradation when the latter reaction was carried out in DMF rather than in C6H6, or even in C6H6 in the

presence of imidazole derivs.

L9 ANSWER 54 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Biosynthesis [of alkaloids]. 1. General
AB A review with 90 refs. including Pinus, Nicotiana, Lycopodium, Lythraceae, Senecio, Erythrina, tropane, Tylophora, Cactus, Amaryllidaceae and ergot alkaloids.

L9 ANSWER 55 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Steroid alkaloids. Preparation of 13β-cyano-18-nor-5α-androstane derivatives from conessine
GI For diagram(s), see printed CA Issue.
AB Derivs. corresponding to 13β-cyano-18-nor-5α-pregnane, especially 13β-cyano-3,3-ethylenedioxy-18-nor-20-oxo-5α-pregnane (I), have been prepared by oxidation of imines derived from conessine with peracids. An attempt was made to prepare corresponding derivs. of 13β-cyano-18-nor-5α-androstane (II) by degradation of the lateral chain at 17. 13β-Cyano-3,3-ethylenedioxy - 18-nor - 20 - oximo - 5α- pregnane, m. 247°, [α] D -7°, treated under conditions for Beckmann rearrangement with POCl3 in C5H5N did not give the expected 17β-acetamidoandrostane. Preliminary expts. carried out with 13β-cyano-18-nor-5α-pregnane-20-one, m. 136-7°, [α]D 20°, and CF3CO2OH in CH2Cl2 in the presence of Na2HPO4 gave 13β-cyano-17β-acetoxy-18-nor-5α-androstane (III), m. 155°, [α]D -33°. Alkaline hydrolysis of III gave 13β-cyano-17β-hydroxy-18-nor-5α-androstane, m. 180°, [α]D 7°, oxidized by CrO3 in C5H5N to 13β-cyano-18-nor-5α-androstan-17-one, m. 141°, [α]D 46°. These conditions are not applicable to I. To prepare derivs. of II substituted at 3 and 17, 3β-hydroxy-N-demethyl-5α-conan-20-ene was used. This **pyrroline** in CH2Cl2 treated with nitroperbenzoic acid gave the **oxirane** (IIIa), m. 166°, [α]D 26°. The nitrile (IIIb) was prepared directly from the **pyrroline** by the action of p-nitroperbenzoic acid; the mixture obtained, treated with hot Ac2O, gave 3β-acetoxy-13β-cyano-18-nor-5α-pregnan-20-one (IV), m. 182°, [α]D 4°. IV in CH2Cl2, treated with excess trifluoroperacetic acid gave 3β,17β-diacetoxy-13β-cyano-5α-androstane (V), m. 142, [α]D -34°. V was hydrolyzed with NaOH in MeOH to 3β,17β-dihydroxy-18-nor-5α-androstane (VI), m. 198°, [α]D 5°. Oxidation of VI with CrO3 in C5H5N gave 13β-cyano-18-nor-5α-androstane-3,17- **dione**, m. 162°, [α]D 69°. The structures of these compds. have been established by elementary analysis, mass spectrometry, and ir and N.M.R. spectra.

L9 ANSWER 56 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Some studies of the formation and structure of melanins
AB In addition to a literature review on the subject (25 references), studies are described of the formation of melanins (I), (a) enzymically, and (b) by autoxidn. from 2,3-(HO)2C6H3CH2CH(CO2H)NH2 (II) and 2,3-(HO)2C6H3CH2CH2NH2 (III). When II and III were labeled with D in the α or β position of the side chain and then converted to I, large retention of D was observed in the I. This suggests that the I are not polymers composed entirely of indole-5,6-quinone, but that they also contain uncyclized units of the precursors (or quinones derived from these) or (more probably) units of 2,3-dihydroindole-5,6-quinone. When I prepared from II-carboxy-14C was oxidized, the resulting **pyrrole**-2,3,5-tricarboxylic acid was radioactive while the **pyrrole**-2,3-dicarboxylic acid was inactive.

L9 ANSWER 57 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI 10α-Methyl-9β-hormonal steroids
AB 4,7,22-Lumistatrien-3-one (125 g.) in 2.2 l. iso-PrOH previously saturated with dry HCl, dry HCl passed through the solution for 0.5 hr., and worked up

gave 80.5 g. lumista-4,6,22-trien-3-one (I), m. 101-2° (ligroine), [α]25D -632° (all rotations in CHCl3 unless otherwise mentioned). I (3 g.) in 300 ml. Et2O added to 450 ml. liquid NH3, treated with 420 mg. Li in NH3 and the product chromatographed on Al2O3 gave 2.43 g. lumista-4,22-dien-3-one (II), m. 122-4° (Me2CO), [α]20D -125°. II(20g.)in 750 ml. CH2Cl2 and 5.75 ml. C5H5N ozonized 4.5 hrs. at -80 gave 10.1 g. 3-oxo retrobisnor-4-cholen-22-al (III), m. 122-30° (ligroine), [α]23D -144°. III (450 mg.) in 15 ml. CHCl3 and 25 ml. AcOH oxidized 16 hrs. at 30° with 200 mg. CrO3 and 0.2 ml. H2O gave 340 mg. 3-oxoretrobisnor-4-cholenic acid (IV), m. 202-4° (Et2O). Alternatively a solution of 450 mg. of an ozonide of II in 25 ml. CH2Cl2 left overnight at 30° with 200 mg. CrO3 in 25 ml. AcOH gave 150 mg. IV. III (300 mg.), 0.11 ml. piperidine, and 1 to 5 mg. p-MeCoH4SO3H refluxed 3 hrs. in 5 ml. dry C6H6 gave 185 mg. 22-(N-piperidyl)retrobisnorchola-4,20(22)dien-3-one (V), m. 94-6° (MeOH). Other samples of V m. 114-15° (probably due to cis-trans isomerism). Alternatively 10 g. III refluxed 3 hrs. in 180 ml. C6H6 with 3.8 ml. piperidine and 30 mg. p-MeC6H4SO3H gave 9.3 g. V. III (1 g.) refluxed with 0.5 g. fused NaOAc and 50 ml. Ac2O gave 22-acetoxyretrobisnorchola-4,20(22)-dien-3-one (VI). V (300 mg.) in 4.5 ml. C6H6 added in 45 min. at -5° to +5° to 453 mg. Na2Cr2O7.2H2O in 4.5 ml. AcOH and 3 ml. C6H6 and the product worked up gave 150 mg. retroprogesterone (VII), m. 163-4° (CH2Cl2-ligroine), [α]20D - 62°. III treated with NaOAc in Ac2O gave VI and VI ozonized, decomposed, and hydrolyzed gave VII. VII (10 g.) in 79 ml. C6H6 stirred 1.5 hrs. with NaOMe in diethyl oxalate and some C6H6 gave 10.8 g. Na enolate of 21-ethoxyoxalylretroprogesterone (VIII). VIII in 150 ml. MeOH treated 40 min. at -20 with 5.9 g. iodine in 210 ml. MeOH, mixture stirred 1.5 hrs., and the iodine compound decomposed with NaOMe solution gave 5.55 g. 21-iodoretroprogesterone (IX). IX (5.55 g.) refluxed 18 hrs. in 200 ml. Me2CO with 12 g. KOAc and chromatographed on Al2O3 gave 335 mg. retrodeoxycorticosterone acetate, m. 165-8° (alc.). V (9.6 g.) in 475 ml. CH2Cl2 treated dropwise at -55°with 4.08 g. Br in 50 ml. CH2Cl2, the dibromo compound stirred 2 hrs. at 20°, the 20-bromo derivative heated 1 hr. at 70° with 70 ml. C5H5N, then 0.5 hr. at 100°, and worked up gave 6 g. 3-oxoretrobisnorchol-4,17(20)-dien-22-al (X), m. 155-9° (Me2CO-alc.), [α]23D -138°. III (7.7 g.) in 100 ml. CCl4 treated with 48 ml. Br solution in CCl4 (0.515 mole/ml.) and 3 g. CaCO3 and then treated with C5H5N gave 7.15 g. X. X (5 g.) suspended with 8 g. NaCN in 50 ml. MeOH at -20°, left 2 hrs. at 20°with 7.1 ml. AcOH, then 40 hrs. at 5°, and worked up gave the 22-HCN addition product of X which treated at -80° with O3 gave 1.48 g. retroandrost-4-en-3,17-**dione** (XI), m. 154-6° (alc.). XI (3.03 g.) in 25 ml. C6H6 and 25 ml. Et2O left 16 hrs. with 1.61 g. K in liquid NH3 which had been treated with CH.tplbond.CH gave 1.95 g. 17α-ethynylretrotestosterone (XIa), m. 195-6° (hexane), [α]20D -219. 3-Oxoretrobisnorchola-4,6-dien-22-al (XII) (3.5 g.) in 50 ml. C6H6 refluxed 2.5 hrs. with 1.27 ml. piperidine and 20 mg. p-MeC6H4SO3H gave 2.1 g. 22-(N-piperidyl)retrobisnorchola-4,6,20(22)-trien-3-one (XIII), m. 135-6° (Me2CO). XIII oxidized with Na2Cr2O7 in AcOH gave 6-dehydroretroprogesterone (XIV), m. 168-9° (Me2CO). Lumisterone (3.95 g.) in 150 ml. CH2Cl2 and 0.81 ml. C5H5N treated with O3 gave 3.11 g. 3-oxoretrobisnorchola-4,7-dien-22-al (XV), m. 196-200° (CH2Cl2-Me2CO). XV treated with piperidine and then oxidized with Na2Cr2O7 gave 7-dehydroretroprogesterone (XVI). By isomerization of the 3-oxo-4,7-dehydro system of XVI with dry HCl XIV was obtained. VII (7.5 g.) in 500 ml. tert-BuOH refluxed 5 hrs. with 12.75 g. chloranil and the product chromatographed on Al2O3 gave XIV. I (3.95 g.) ozonized as described above gave 3.08 g. XII, m. 153-5° (Me2CO). 3-Oxoretrobisnorchol-4,20(22) dien-22-al (0.978 g.) in 10 ml. C6H6 kept 4 hrs. at 0° with 1.2 g. monoperphthalic acid in 25.5 ml. EtOAc gave 0.88 g. 17(20)epoxy-20-formyloxyretropregn-4-en-3-one (XVII). Hydrolysis of XVII with 2N NaOH gave 17α-hydroxyretroprogesterone (XVIII), m. 222-5° (alc.). XIII (6.5 g.) treated with Br and then with C5H5N gave 2.41 g. retrobisnorchola-4,6,17(20)-trien-3-one-22-al (XIX), m.

217-19° (Me2CO). XIX (15 g.) in 150 ml. EtOAc and 150 ml. C6H6 treated with 20.2 g. monoperphthalic acid in 450 ml. EtOAc and left 16 hrs. gave 16.4 g. resinous epoxy-20-formyloxy compound which treated 1.5 hrs. at 30° with 2N NaOH gave 5.69 g. 6-dehydro-17α-hydroxyretroprogesterone (XX). XIX (3.7 g.) treated as above with 5.9 g. NaCN and MeOH followed by ozonization gave 1.2 g. retroandrosta-4,6-diene-3,17-**dione**, m. 189-90° (Me2CO). XVIII (220 mg.) and 220 mg. p-MeC6H4SO3H in 15 ml. AcOH kept 18 hrs. at room temperature gave 130 mg. 3,17-diacetate of XVIII, m. 217-18° (CH2Cl2-MeOH). XVIII (0.5 g.) similarly treated but in less Ac2O and the product fractionally crystallized gave 260 mg. 17α-acetoxyretroprogesterone, m. 171-3° (MeOH). XVIII (900 mg.) treated with caproic anhydride and p-MeC6H4SO3H, then with 0.3 ml. concentrated HCl in 20 ml. alc., and the product chromatographed gave

mg. 17-caproate of XVIII, m. 50-3° (hexane). Many esters of XVIII were similarly preparing XVIII (0.495 g.) in tert-BuOH treated with chloranil gave 50 mg. XX, m. 242-5° (alc.-hexane). 6-Dehydro-17α-acetoxyretroprogesterone, m. 181-3°, was similarly prepared Retroprogesterone hydroxylated with Rhizopus nigricans gave a hydroxyretroprogesterone, m. 217-18°, and 17α,21-dihydroxyretroprogesterone (XXa) incubated with Aspergillus ochraceusgave retrohydrocortisone, m. 269° (decomposition). XIa (1.88 g.) in 50 ml. C5H5N hydrogenated over 2 g. Pd-CaCO3 gave 1.17 g. 17α-vinylretrotestosterone, m. 143.5-5.5° (Me2CO-hexane). VII (5 g.) in 250 ml. C6H6 refluxed 7 hrs. with 4 g. dichlorodicyanobenzoquinone and the product chromatographed on silica gel gave 2.14 g. 1-dehydroretroprogesterone, m. 154-5.5° (Me2CO-hexane). XIV (2.5 g.) gave 208 mg. dioxime, m. 279-82° (tetrahydrofuran-ligroine). I (75 g.) and 55 ml. HCO2Et in 1.2 l. C6H6 kept 3 days at room temperature with 16.5 g. NaH and the Na salt converted to the free alc. gave 2-hydroxymethylenelumista-4,6,22-trien-3-one (XXI) as the hydrate, m. 119-22°, anhydrous form m. 122-3.5°. Similarly, II gave 2-hydroxymethylenelumista-4,22-dien-3-one (XXII), m. 134-5°. XXI (108 g. of Na salt) in 3.2 l. alc. treated 3.5 to 4.5 hrs. at 10° with perchloryl fluoride gave 71 g. 2-fluorolumista-4,6,22-trien-3-one (XXIII), m. 158-60° (MeOH), [α]27D -635° (alc.). XXII similarly gave 2-fluorolumista-4,22-dien-3-one. XXIII (30.5 g.) in 610 ml. CH2Cl2 and 10 ml. C5H5N treated with O3 at -80° gave 16.6 g. 2-fluororetrobisnorchola-4,6-dien-3-on-22-al (XXIV), m. 183-5° (CH2Cl2-Et2O). XXIV (2.08 g.) similarly treated with piperidine and p-MeC6H4SO3H gave 2-fluoro-22-(N-piperidyl)-retrobisnorchola-4,6,20(22)-trien-3-one, which with CrO3 gave 2-fluoro-6-dehydroretroprogesterone, m. 153-4° (alc.). Retropregnane-3,20-**dione** (XXV) (300 mg.) in alc. treated 3 hrs. at -20° with 36.6 mg. CaCl2.2H2O and 16.3 mg. NaBH4 gave retropregnan-3-ol-20-one, m. 167-71° (alc.-E+2O). VII (2.826 g.) in 150 ml. dioxane shaken with excess H over 0.3 g. 10% Pd-C in the presence of 0.6 g. KOH in 9 ml. MeOH gave XXV, m. 115-16° (E+2O-hexane). XIV (5 g.), 7.5 g. chloranil, and 25 g. CaCO3 refluxed 3 hrs. with 170 ml. isoamyl alc. and chromatography of the product gave XIV and 150 mg. 1,6-bisdehydroretroprogesterone (XXVI). XIV (5 g.) and 5.1 g. dihydroquinone in 250 ml. C6H6 refluxed 6 hrs. gave 1.52 g. XXVI, m. 143-3.5° (Me2CO-hexane). VII enol acetate (7.5 g.) and dioxane treated at room temperature with perchloryl fluoride gave 185 mg. 6α-fluororetroprogesterone (XXVII), m. 150-1° (Me2CO-hexane), 1.16 g. 6β-fluororetroprogesterone (XXVIII), m. 163-5° (MeOH), and 77 mg. 6-hydroxyretroprogesterone, m. 220-2° (Me2CO). XXVII (50 mg.) in 10 ml. CHCl3 treated 1 hr. with passage of dry HCl gave XXVIII. XVIII (1 g.) in 15 ml. tetrahydrofuran and 2.5 ml. MeOH treated at -4° to 0° with 1.5 g. iodine and the product refluxed with KOAc in Me2CO gave 772 mg. 17α,21-dihydroxyretroprogesterone 21-acetate (XXIX), m. 218-238° (decomposition) (Me2CO). XX (1 g.) in 15 ml. tetrahydrofuran and 2.5 ml. MeOH similarly treated with iodine and the product refluxed with KOAc in Me2CO gave 915 mg. 6-dehydro-17α,21-dihydroxyretroprogesterone 21-acetate, m. 238.5-44° and

257-9° (decomposition). XXIX (1.2 g.) in 30 ml. MeOH stirred 2 hrs. at 24° with 216 mg. K_2CO_3 in 6 ml. H_2O gave 897.5 mg. XXa. XIa (3.12 g.) in 250 ml. dioxane reduced with H over $PdCaCO_3$ and the product chromatographed on silica gel gave 300 mg. 17α-ethyl-5-retroandrostan-17-ol-3-one (A isomer), m. 125-6.5° (Et_2O-petr. ether) and 828 mg. B isomer, m. 125-6.5°. VII was converted to its 3-enol acetate, m. 90-2° (MeOH). Retroandrosta-4,6-diene-3,17-**dione** (2.35 g.) in 70 ml. 2:1 mixture C_6H_6-Et_2O stirred 0.5 hr. at -80° with 1.28 g. K in 50 ml. liquid NH_3 previously treated with CH.tplbond.CH gave 6-dehydro-17α-ethynylretrotestosterone, m. 205-7° (Me_2CO-hexane). IX (6.6 g.) in 200 ml. MeCN and 5.72 g. AgF stirred 25 hrs. at 45° gave 21-fluororetroprogesterone, m. 173-5° (alc.-Me_2CO). XIV (10 g.) in 70 ml. C_6H_6 stirred 1.5 hrs. with 8.5 ml. $(CO_2Et)_2$ and 10.5 ml. of a 3.45N NaOMe solution in MeOH, 70 ml. C_6H_6, and 3.2 ml. alc. gave 12.2 g. Na enolate of 21-ethoxyoxalyl-6-dehydroretroprogesterone (XXX). XXX in 170 ml. MeOH treated at -25° with 7.2 g. iodine gave 12-iodo-6-dehydroretroprogesterone (XXXI). XXXI refluxed 5 hrs. with KOAc in Me_2CO, H_2O, and AcOH gave 6-dehydro-21-acetoxyretroprogesterone, m. 194.5-7.5°. XIV (937 mg.) in 125 ml. CCl_4 treated in 50 min. with 0.5 g. Br in 10 ml. CCl_4 gave 4-bromo-6-dehydroretroprogesterone m. 121-2° (MeOH) (decomposition). XIV with Cl similarly afforded 4-chloro-6-dehydroretroprogesterone, m. 185-6°. 6-Chlororetroprogesterone (XXXII) (700 mg.) and 1 g. chloranil refluxed 30 hrs. in 100 ml. tert-BuOH gave 6-chloro-6-dehydroretroprogesterone, m. 165-6° (alc.). 3-Acetoxyretropregna-3,5-dien-20-one (XXXIII) (1.85 g.) in 30 ml. Et_2O, 4 g. KOAc, 60 ml. 85% AcOH treated with 375 mg. Cl in 9.4 ml. AcOH gave XXXII, m. 197-9.5° (EtOAc), and 3,6,20-trioxoretropregnane, m. 201-3°. 6-Bromoretroprogesterone was similarly prepared, m. 138-40° (decomposition). XIV (5 g.) reduced with $NaBH_4$ in alkali gave retropregna-4,6-diene-3,20-diol (XXXIV). XXXIV in C_6H_6 refluxed with 50 g. MnO_2 gave 3.27 g. retropregna-4,6-dien-20-ol-3-one, m. 198-8.5° (Me_2CO), and a second C-20 isomer, m. 173-5°. Retropregna-4-en-20-ol-3-one (XXXV) treated with NaH and HCO_2Et and the Na product acidified with 5% HCl gave 2-hydroxymethyleneretropregn-4-en-20-ol-3-one, m. 94-9° (Et_2O), [α]21D -155° (alc.). VII (2 g.) in 40 ml. tetrahydrofuran reduced with $LiAlH_4$ gave retropregn-4-ene-3,20-diol and this product refluxed with MnO_2 in C_6H_6 gave 1.69 g. XXXV, m. 174-6° (Me_2CO-hexane). XIV (1 g.) in 10 ml. CH_2Cl_2 treated with alc.-HCl gave 3-ethoxyretropregna-3,5,7-trien-20-one, m. 115-16° (MeOH). XXXII (7.5 g.) in 200 ml. AcOH refluxed 4.5 hrs. with 21 g. KOAc gave 2-acetoxyretroprogesterone, m. 195.5-7.0° (alc.). XXXIII treated with monoperphthalic acid in EtOAc gave 6-hydroxyretroprogesterone (XXXVI). Acetylation of XXXVI gave 6-acetoxyretroprogesterone, m. 177-8.5° (alc.). XX was converted into the 17-caproate, m. 110-12.5° (E_2O-hexane). 3,17-Diacetoxyretropregna-3,5-dien-20-one (13.2 g.) in 950 ml. dioxane and 40 ml. H_2O treated 1 hr. at room temperature with passage of perchloryl fluoride gave 6α-fluoro-17α-acetoxyretroprogesterone, m. 177-9° (Me_2CO-hexane), and 6β-fluoro-17α-acetoxyretroprogesterone, m. 197.5-8.5° (Me_2CO), plus 3,6,20-trioxoretropregnan-17α-ol 17-acetate, m. 241-4° (Et_2O-C_6H_6-Me_2CO). XIV (25 g.) treated with BzO_2H gave 6,7-oxidoretroprogesterone (XXXVII), m. 187-90° (EtOAc), and some 6-chloro-7-hydroxyretroprogesterone (XXXVIII) due to splitting of the epoxy bond of XXXVII during chromatography. XXXVIII treated with HCl 3 hrs. at room temperature gave 6-chloro-6-dehydroretroprogesterone. XXVIII (4 g.) and 4 g. dichlorodicyanobenzoquinone in C_6H_6 refluxed 7.5 hrs. over 0.4 g. p-nitrophenol gave 2 g. 1-dehydro-6β-fluororetroprogesterone, m. 208-11° (EtOAc). 17α-Acetoxyretroprogesterone in MeOH treated 6 days with CuBr gave 6-dehydro-6-methoxy-17α-acetoxyretroprogesterone, m. 275-80° (alc.). XIV (3 g.) in 3 ml. thioacetic acid refluxed 2.5 hrs. gave 7-acetylthioretroprogesterone, m. 133-5° (Me_2CO-hexane). VII similarly treated with CuBr gave 6-dehydro-6-methoxyretroprogesterone, m. 206-8°. XI (3 g.) in 30 ml. MeOH refluxed 10 min. with 1.6 ml. **pyrrolidine** gave 3.31 g.

3-(N-**pyrrolidino**)retroandrosta-3,5-dien-17-one (XXXIX). XXXIX (3.3 g.) refluxed 5 hrs. with a solution containing methallyl-magnesium chloride and worked up gave 2.52 g. 17α-(2-methallyl)retrotestosterone, m. 91-3° (MeOH). Dried sample from Et2O m. 106-8°. I (60 g.) and 6 g. CuCl in 500 ml. tetrahydrofuran stirred 3 hrs. with solution prepared from 100 ml. MeBr, 25 mg. Mg, and 5 g. CuCl in 200 ml. tetrahydrofuran gave 29 g. 7-methyllumista-4,22-dien-3-one (XL), m. 94.5-5.5° (ligroine), [α]22D -150.5°. XL upon ozonization gave 3-oxo-7-methylretrobisnorchol-4-en-22-al (XLI), m. 161.5-2.0°, [α]23D -148. XLI (4.65 g.) in 100 ml. C6H6 refluxed 5 hrs. with 2 ml. piperidine and 2 mg. p-MeC6H4SO3H gave 7-methyl-22-(N-piperidyl)-retrobisnorchola-4,20(22)-dien-3-one (XLII), m. 153.5-4.5°, [α]23D -120°. XLII (1.96 g.) treated with Na2CR2O7 in AcOH gave 7-methylretroprogesterone, m. 206-8°, [α]25D -57°. XXXIX treated with CH2:CHCH2MgCl gave 17α-allylretrotestosterone, m. 74-8°. XX (1 g.) heated 45 min. at 80° with 3.3 g. trimethylacetic acid and 1 ml. trifluoroacetic anhydride gave 6-dehydro-17α-hydroxyretroprogesterone 17-pimalate, m. 214-16°. 17α-Acetoxyretroprogesterone (4 g.) refluxed 15 hrs. with 2.7 g. dichlorodicyanobenzoquinone in 200 ml. C6H6 gave 1-dehydro-17α-acetoxyretroprogesterone, m. 183-4.5°. XIa treated with Ac2O-p-MeC6H4SO3H and then with concentrated HCl in MeOH gave 17α-ethynylretrotestosterone 17-acetate, m. 183-4° (Me2CO). VII by hydroxylation (microbiol.) gave 16α-hydroxyretroprogesterone (XLIII), m. 172.5-4.5°, [α]25D -92.3°. Dehydration of XLIII gave 16-dehydro retroprogesterone, m. 165-7°. Microbiol. hydroxylation of VII gave 15α-hydroxyretroprogesterone, m. 203-5°, [α]D -23°. Oxidation of 11,17α,21-trihydroxyretroprogesterone 21-acetate with CrO3 gave retrocortisone 21-acetate, m. 275° (decomposition). Microbiol. hydroxylation of XIV gave 6-dehydro-16α-hydroxyretroprogesterone (XLIV), m. 200-3°, [α]D -526°. Dehydration of XLIV gave 6,16-bisdehydroretroprogesterone, m. 163-5°. Hydroxylation of VII gave 11-hydroxyretroprogesterone (XLV). Oxidation of XLV with CrO3 gave 11-oxoretroprogesterone, m. 158-60°. Hydroxylation of XVIII gave 11,17α-dihydroxyretroprogesterone (XLVI), m. 202-6.5° (decomposition), [α]D -118°. XLVI oxidized as above gave 11-oxo-17α-hydroxyretroprogesterone, m. 240-5°. XXIII was converted into 2-fluoro-6-dehydro-17α-acetoxyretroprogesterone, m. 204-5°. Degradation of the side-chain of 2-fluorodihydroisolumisterone gave 2-fluororetroprogesterone, m. 162-4°. II was converted to 2-(ethoxyoxalyl)lumista-4,22-dien-3-one then to 2-methyllumista-4,22-dien-3-one (XLVII). XLVII ozonized, treated with Ac2O, and oxidized gave 2-methylretroprogesterone, m. 126-7°. Degradation of the side chain of 2-methyllumista-4,6,22-trien-3-one gave 2-methyl-6-dehydroretroprogesterone, m. 168.5-70.0°. Retroandrost-4-en-17-one (XLVIII) treated with CH2:CHCH2MgCl gave 17α-allylretroandrost-4-en-17-ol, m. 79-86°. XLVIII with KC.tplbond.CH in iso-PrOH gave 17α-ethynylretroandrost-4-en-17-ol, m. 74-5°. Treatment of the Na enolate of the 21-ethoxy oxalate of XXVI with perchloryl fluoride in MeOH and NaOMe gave after refluxing with KOAc 21-fluoro-1,6-bisdehydroretroprogesterone, m. 154-5°. XI (1.13 g.) reduced with 550 mg. LiAlH4 gave retroandrost-4-en-3,17β-diol (XLIX), m. 117-18° (ligroine). Crude XLIX shaken 17 hrs. in 60 ml. CHCl3 with 6 g. MnO2 gave retrotestosterone (L), m. 115-6° (E+2O), [α]23D -154°. L gave the β-phenylpropionate, m. 73-4° (MeOH). L (5 g.) treated as above with chloranil 1.43 g. 6-dehydroretrotestosterone (LI), m. 174-5° (E2O). LI (360 mg.) afforded 233 mg. propionate, m. 115-17° (MeOH). L (0.5 g.) treated with 0.5 g. Li in 75 ml. NH3 and 50 ml. E2O and the product esterified gave 270 mg. bis(3,5-dinitrobenzoate) of retro-5-androstane-3,17β-diol, m. 237-42°(CH2Cl2-Me2CO). L (1 g.) in 35 ml. C6H6 refluxed 48 hrs. with 1 g. SeO2 and 0.6 ml. H2O and the product chromatographed on

Al2O3 gave 98 mg. 1-dehydroretrotestosterone, m. 175-7° (hexane-CH2Cl2). L (1.14 g.) was converted into enol of 2-(ethoxyoxalyl)retrotestosterone (LII). LII (1.3 g.) refluxed 18 hrs. with 2 ml. MeI in 25 ml. Me2CO and 1 g. K2CO3 and chromatographed on Al2O3 gave 207 mg. 2-methylretrotestosterone, m. 177-9.5° (Et2O-hexane). Retroandrosta-4,6-dien3,17-**dione** (LIIa) treated with LiAlH4 gave retroandrosta-4,6-diene-3,17β-diol (LIII), m. 140-4 (decomposition). Crude LIII refluxed 30 hrs. with MnO2 in C6H6 gave 3 g. LI. 6-Bromoretrotestosterone 17-acetate treated with C5H5N gave 17-acetate of LI, m. 131-3° L (1 g.) and 0.005 ml. concentrated H2SO4 refluxed 3 hrs. with 5 ml. isopropenyl acetate gave 0.9 g. 3,17β-diacetoxyretroandrosta-3,5-diene, m. 118-19 (MeOH). L (1g.)added to 0.4 g. K in 20 ml. tert-BuOH, left 3.5 hrs. at room temperature with 1.3 ml. MeI gave 4,4-dimethylretroandrost-5-en-17β-ol-3-one, m. 152.5-3.5°. L gave thep-hexyloxyphenylpropionate and propionate (LIV), m. 107-8°.

LIV acetylated with isopropenyl acetate in the presence of traces of concentrated H2SO4 gave 3-acetoxyretroandrosta-3,5-dien-17β-ol 17-propionate, m. 102-4°. 6-Bromoretrotestosterone 17-acetate (410 mg.) and 1.3 g. KOAc in 10 ml. AcOH refluxed 4 hrs. gave 2-hydroxyretrotestosterone 2,17-diacetate, m. 184-6°. 3,17-Diacetoxyretroandrosta-3,5-diene treated with KOAc in AcOH, then with Br in AcOH, and worked up gave 6-bromoretrotestosterone 17-acetate, m. 130° (decomposition). 3,17°-Diacetoxyretroandrosta-3,5-diene (4 g.) in 178 ml. EtOAc containing 14.3 mg. monoperphthalic acid/ml. left overnight at 5° gave mixture (LV) of 6α- and 6β-hydroxyretrotestosterone 17-acetate, m. 167-70°. LV (2.6 g.) in 10 ml. C5H5N and 10 ml. Ac2O left 20 hrs. at room temperature and the product separated gave one isomer of 6,17-diacetoxyretrotestosterone, m. 178-80°, and the other isomer, m. 116-17°. LI was converted to the 17-palmitate, m. 58.5-9.0°. L treated with NaH and HCO2Et and then with 5% HCl gave 2-hydroxymethyleneretrotestosterone (LVI), m. 98-120° (aqueous alc.). LVI (5 g.) in 13 ml. alc. refluxed 3 hrs. with 2.5 ml. N2H4.H2O in 40 ml. alc. gave 3.5 g. 17β-hydroxyretroandrost-4-eno[3,2-c]pyrazole, m. 259-63°, [α]24D -149° (alc.). LI (2 g. (in 10 ml. pyridine left 18 hrs. at room temperature with 2.5 g. p-hexyloxyphenylpropionyl chloride gave 3.9 g. resinous 6-dehydroretrotestosterone 17-(p-hexyloxyphenylpropionate). LI treated 16 hrs. at 60**.degree** . with succinic anhydride gave the 17-hemisuccinate, **m.** 178-93.5-201.5-203.5°. LI also gave the 17-phenylpropionate, m. 93-4° (MeOH). LIIa treated with Br in CCl4 gave 4-bromoretroandrosta-4,6-dien-3,17-dione, m. 130-50°. L 17-propionate (1.2 g.) in 150 ml. C6H6 treated with 9 ml. (CH2OH)2 gave 3,3-ethylenedioxyretroandrosta-3,5-dien-17β-ol-17-propionate, m. 66-8β. XXXIX (3 g.) treated with MeMgBr gave 17α-methylretrotestosterone (LVII), m. 133-4°. LIIa similarly gave 3-ethoxyretroandrosta-3,5,7-trien-17-one, m. 118-19.5°. LIIa (1 g.) in 15 ml. CH2Cl2 left 0.5 hr. at 0° with dry HCl in MeOH gave 404 mg. 3-methoxyretroandrosta-3,5,7-trien-17-one, m. 139-40°. L (2.5 g.) converted to the 17-hexahydrobenzoate, m. 71-3° (petr. ether). LVII (2 g.) and dichlorodicyanobenzoquinone in C6H6 refluxed 7 hrs. gave 1-dehydro-17α-methylretrotestosterone, m. 163-4°. XI treated with isopropenyl acetate gave 3-acetoxyretroandrosta-3,5-dien-17-one, m. 142-3°. L (1.564 g.) in 6.25 ml. C5H5N treated 24 hrs. at room temperature with 1.56 g. p-toluenesulfonyl chloride gave the 17-tosylate, m. 164.5-5.5°. The tosylate treated with KOAc in HCONMe2 and the resin hydrolyzed with KOH solution gave retroandrosta-4,16-dien-3-one and L. L was converted into the 17-acetate, m. 128.5-30.0°. 3,17β-Diacetoxyretroandrosta-3,5-diene (10.3 g.) treated in dioxane with perchloryl fluoride and chromatographed on silica gel gave 6α-fluororetrotestosterone 17-acetate, m. 129.5-30.5°. Microbiol. hydroxylation of L gave 16α-hydroxyretrotestosterone, m. 210-12°, [αID -167°. XXIII converted into 2-fluororetrobisnorchol-3-one-4-en-22-al, then into 2-fluororetrobisnorchol-3-one-4,17(20)-dien-22-al,

2-fluororetroandrost-4-en-3,17-dione, 2-fluororetroandrost-4-en-3,17-diol, 2-fluororetrotestosterone, and finally 2-fluoro-6-dehydroretrotestosterone, m. 90-5° and 142-3.5°. XI reduced with NaBH4 in alc.-H2O gave 3,17β-dihydroxyretro-5-androst-4-ene and 8,17β-dihydroxyretroandrostane (LVIII), m. 156-8°. LVIII oxidized with CrO3 in Me2CO containing H2SO4 gave retro-5-androstane-3,17-dione, m. 114-15.5°. 17α-Methylretroandrost-4-en-17-ol was obtained by treatment of retroandrost-4-en-17-one (LIX) with MeMgI. L (2 g.) in 3 ml. Et2O and 6.5 ml. AcOH stirred 1 hr. with 0.72, ml. 1,2-ethanedithiol and 0.85 ml. BF3.Et2O gave 3-ethylene dithioketal of L, m. 166-7.5°. This ketal (0.5 g.) in 2.5 ml. tetrahydrofuran added to 15 ml. liquid NH3 and 5 ml. tetrahydrofuran, stirred 15 min. with 0.4 g. L gave 3-deoxyretrotestosterone (LX). LX oxidized with CrO3 in Me2CO gave LIX, m. 89-90.5°. L with AcCl gave the 17-acetate, m. 113-14.50. XLII (1 g.) in 50 ml. CH2Cl2 treated in 20 min. at -55° with 0.15 ml. Br in 6 ml. CH2Cl2, mixture heated to 0°, and product heated with C5H5N for 1 hr. at 70° gave 7-methylretrobisnorchola-4,17(20)-dien-3-on-22-al (LXI), m. 182-3.5°. LXI suspended in MeOH treated with NaCN, AcOH, and MeOH 2 hrs. from -20° to +5° and kept 40 hrs. at 5° gave 7-methylretroandrost-4-ene-3,17-dione (LXII), m. 196-7°. LXII was reduced to give 7-methylretroandrost-4-ene-3,17β-diol (LXIII), m. 80-95°. LXIII oxidized as above gave 7-methylretrotestosterone, m. 146.5-50.0°. 3,17β-Diacetoxyretroandrosta-3,5-diene (3 g.) in 60 ml. Et2O treated with 6.4 g. KOAc in 120 ml. 85% AcOH, and treated 5-10 min. at 0° with 0.57 g. Cl gave 6-chlororetrotestosterone 17-acetate, m. 176-8°. II treated with Et orthoformate in C6H6 and alc. gave 3-ethoxylumista-3,5,22-triene (LXIV), m. 76-7.5° (alc.). LXIV (12.7 g.) in 60 ml. dioxane and 4.8 ml. C5H5N left 45 hrs. at room temperature with 20 g. CBr4 gave 7.46 g. 6-tribromomethyldihydroisolumisterone (LXV), m. 132-3.5° (Me2CO-MeOH). LXV (100 mg.) in 15 ml. alc. heated with 15 ml. of a strong anion exchange resin gave 6-dibromomethylenedihydroisolumisterone, m. 100-2.5°, [α]23D 10°. XI was converted into 3-(1-pyrrolidino)retroandrosta-3,5-dien-17-one (LXVI). LXVI treated with CH2:CMeCH2MgCl gave 17α-(2-methallyl)retrotestosterone, m. 106-8°. Similarly LXVI gave 17α-allylretrostesterone, m. 76-8°. Retroandrosta-4,6-diene-3,17-dione was converted into 3,7-di(1-pyrrolidino)retroandrosta-3,5-dien-17-one, and then alkylated to give 6-dehydro-17α-(2-methallyl)retrotestosterone. Many related compds. were prepared by the above described procedures.

L9 ANSWER 58 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Antibiotic inhibition of algal growth
AB A study of antibiotic inhibitions of Chlorella pyrenoidosa (Wis. 2005) and Scenedesmus obliquus (Indiana 393) growing heterotrophically in suspension culture showed that only those antibiotics inhibiting gram-neg. bacteria and those inhibiting fungi were effective against these algae. The most active antibiotics were amphotericin B, cycloheximide, hygromycin B, kanamycin, nystatin, and paromomycin. Of 24 antibiotics inhibiting only gram-pos. bacteria, only thiostrepton had significant inhibitory activity for one of these 2 representatives of the Chlorophyceae. Significant differences were noted in the responses of these 2 algae to many of the 60 antibiotics tested. 1-Hydroxy-2-(1H)-pyridinethione (Omadine), which had a min. inhibitory concentration of 0.1 ppm., was as inhibitory as the "active" antibiotics, and was more active than the algicide dodecylbenzyltrimethyl-ammonium chloride.

L9 ANSWER 59 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN
TI Steroid alkaloids. XXVIII. New method of preparation of 18-substituted pregnane derivatives from conessine
GI For diagram(s), see printed CA Issue.
AB 20(N)-Conanene derivs. treated with 1 mole-equivalent peracid gave the corresponding **oxiranes**, which were converted into 18-substituted pregnane derivs. N-Demethyl-5α-conan-20(N)-ene (1 g.) in 20 cc.

CHCl3 treated with stirring with 0.593 g. p-O2NC6H4CO2OH (I) in portions at 15-min. intervals and stirred 15 min. yielded 0.99 g. N-demethyl-20,N-oxido-5α-conan-3-one (II), m. 140-1° (95% EtOH) (sublimed at 135°/0.01 mm.), [α]20D 53° (c 1.24) (all rotations in CHCl3). II (1.67 g.) in 10 cc. MeOH and a few crystals p-MeC6H4SO3H refrigerated 3 hrs. yielded 1.46 g. 3,3-dimethoxy-20,N-oxido-N-demethyl-5α-conanine (III), m. 209-10° (Me2CO), [α]20D 31° (c 1). III (1.02 g.) in 20 cc. CH2Cl2 and 1 g. Na2CO3 treated with stirring with 0.77 g. I gave 0.856 g. 3,3-dimethoxy-18-oximo-5α-pregnan-20-one (IV), decompose .apprx.130° with a change at 85-90° (MeOH or Me2CO), [α]20D 7° (c 1). IV (0.254 g.) in 10 cc. CH2Cl2 treated 5 min. with 10 cc. N HCl gave 0.149 g. 18-oximino-5α-pregnane-3,20-**dione** (V), m. 186-7° (Me2CO). 13β-Cyano-18-nor-5α-pregnane-3,20- **dione** (VI) (1.8 g.) in 30 cc. MeOH stirred with a few crystals p-MeC6H4SO3H yielded 1.32 g. 3,3-dimethoxy-13β-cyano-18-nor-5α-pregnan-20-one (VII), m. 190-1° (MeOH and sublimed in vacuo), [α]20D 17° (c 1.1). VII (0.258 g.) in 20 cc. CH2Cl2 treated 1 hr. with 20 cc. N HCl yielded 0.229 g. VI, m. 192-3° (95% EtOH), [α]20D 41° (c 1.06). N-Demethyl-5α-conan-20(N)-ene (4 g.) in 25 cc. CHCl3 added during 10 min. with stirring to 6 g. I in 130 cc. CHCl3 and stirred 50 min. gave 2.767 g. V, m. 185-6° (Me2CO), containing a small amount of a by-product. V (0.703 g.) in 10 cc. dry C5H5N treated with 0.3 cc. POCl3 gave 0.546 g. VI, m. 182-3°. II (0.5 g.) in 10 cc. CHCl3 and 0.5 g. Na2CO3 treated during 15 min. with 0.426 g. I gave 0.328 g. mixture, m. 199-200° (Me2CO); a 0.966-g. portion treated with 13 cc. dry C5H5N and 0.86 cc. POCl3 gave 0.22 g. VI. VI (1 g.) in 17 cc. tetrahydrofuran added dropwise with stirring at 0° to (tert-BuO)3AlLiH from 0.25 g. LiAlH4 in 10 cc. tetrahydrofuran, stirred 8 min. at 0° and 1 hr. at room temperature, and poured into 100 cc. 40% aqueous KOH gave 0.918 g. lacquer, which dissolved in 170 cc. absolute EtOH and refluxed 15 hrs. with 160 cc. 2N HCl yielded 0.761 g. crude product; the product chromatographed on 22 g. Al2O3 yielded 0.071 g. 5α-pregnan-20β-ol-3-on-18-oic acid 18,20-lactone, m. 246-8° (Me2CO), [α]20D 28° (c 1),and 0.06 g. 5α-pregnan-20α-ol-3-on-18-oic acid 18,20-lactone, m. 176-7° (Me2CO), [α]20D 17° (c 1).

L9 ANSWER 60 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Epoxides by the action of diaryldiazomethanes on ketones

AB A series of aromatic and heterocyclic ketones was converted with Ph2CN2 (I) to epoxides without the occurrence of ring enlargements and chain extensions observed in the reactions with CH2N2. The different mechanism in the addition of I to the CO group and to alkene derivs. is discussed. Isatin (II) (4.9 g.) and 7.0 g. I in 100 cc. C6H6 refluxed 3.5 hrs. yielded 8.4 g. 3,3'-oxido-3-diphenyhnethyloxindole (III) (R = H) (IIIa), m. 238° (PhMe), yellow in concentrated H2SO4. 3-Diphenylmethyleneoxindole (IV) (0.20 g.) in 5 cc. C6H6 and 25 cc. EtOH treated with 5 cc. 4N NaOH and 10 cc. H2O2 12 hrs. at room temperature yielded 0.15 g. IIIa, m. 238° (MePh). Oxindole (1.3 g.) and 3.0 g. BzPh in 20 cc. Me3COH refluxed 7 hrs. with 0.5 g. Na in 50 cc. tert-BuOH gave 2.1 g. IV, yellow crystals, m. 240° (EtOH and then ligroine, b. 100-40°). IIIa (0.8 g.) in 30 cc. AcOH with 1 g. KI refluxed 5 hrs. yielded BzPh, oxindole, m. 120°, and IV, m. 240°. IIIa (0.6 g.) in 25 cc. AcOH refluxed 0.5 hr. with 5 cc. concentrated HCl gave 0.3 g. BzPh and 0.1 g. isoindigo (IVa, R = H) (sublimed in vacuo at 300°). 1-Methylisatin (11.5 g.) and 15 g. I in 150 cc. MePh refluxed 2 hrs. gave 12 g. III (R = Me) (V), m. 176° (EtOH). V (0.5 g.) in 25 cc. AcOH and 10 cc. concentrated HCl refluxed 0.5 hr. gave 0.2 g. BzPh and IVa (R = Me), red needles, m. 265° (EtOH). IIIa (1.5 g.) and 1.5 g I in 50 cc. C6H6 refluxed 24 hrs. and evaporated, and the residue kept 24 hrs. in Et2O at -20° yielded 1.8 g. III (R = CHPh2) (VI), m.155°. II (1.5g.) and 5.0 cc. I in 75 cc. C6H6 refluxed 24 hrs. gave similarly 2.9

g. VI, m. 155° (EtOH). VI (0.30 g.) in a little AcOH refluxed 0.5 hr. with 0.50 g. Na2Cr2O7 gave 0.15 g. N-diphenylmethylisatin, m. 168°. VI (0.47 g.) in 50 cc. EtOH and 30 cc. concentrated HCl refluxed 3 hrs. yielded 50 mg. IVa (R = CHPh2), red crystals, m. 275° (EtOH). Trioxohydrindene (0.9 g.) and 1.25 g. I in 20 cc. C6H6 heated 10 min. after the violent gas evolution had subsided gave 1.7 g. 2,2'-oxido-2-diphenylmethyl-1,3-dioxohydrindene (VII), m. 155°. VII (0.30 g.) in 10 cc. EtOH refluxed with 1 drop concentrated HCl gave 50 mg. hydrindantin. 9-Dibenzoylmethylenexanthene (5.0 g.) in 50 cc. C6H6 and 100 cc. MeOH treated with stirring at room temperature with 5 cc. 4N NaOH and

10

cc. 30% H2O2 and diluted after 1.5 hrs. with 200 cc. H2O yielded 4.9 g. 9,9'-oxido-9-dibenzoylmethylxanthene (VIII), yellow crystals, m. 178° (EtOH). Ph(CO)3Ph (2.70 g.) in 20 cc. dry C6H6 treated with 2.50 g. diazoxanthene (IX) in 200 cc. petr. ether overnight gave 1.88 g. VIII, m. 178° (MeOH). VIII (0.30 g.) in 20 cc. EtOH and 10 cc. C6H6 refluxed 1 hr. with 1 cc. concentrated HCl yielded 0.13 g. xanthone, m. 174° (EtOH). 1,8-Diazafluorenone (0.60 g.) and 0.70 g. I in 25 cc. C6H6 refluxed 5 hrs. and evaporated, and the residue kept in Me2CO 24 hrs. at -20° gave 0.85 g. 9.9'-oxido-9-diphenylmethyl-1,8-diazafluorene (X), m. 211-12° (Me2CO). 9-Diphenylmethylene-1,8-diazafluorene (0.22 g.) in 10 cc. C6H6 and 40 cc. EtOH treated with stirring at room temperature with 10 cc. 4N NaOH and 15 cc. 30% H2O2 overnight, yielded 0.07 g. X, m. 211-12° (Me2CO). X (0.20 g.) in 20 cc. 1:4 concentrated HCl-H2O refluxed 15 min. yielded 95 mg. BzPh; the aqueous phase yielded 70 mg. 1,8-diazafluorenone, m. 210°. I (7.0 g.) in 50 cc. C6H6 added slowly dropwise with stirring to 5.0 g. acenaphthenequinone (XI) in 200 cc. refluxing C6H6, refluxed 2 hrs., filtered from 2.7 g. XI, m. 260°, and cooled gave an addnl. 2.2 g. XI; the mother liquor yielded 3.5 g. benzophenone azine (XII), m. 164°. XI (1.00 g.) in 75 cc. MeOH and 75 cc. hot C6H6 refluxed 1 hr. with 1.20 g. IX in 100 cc. petr. ether yielded 0.90 g. unreacted XI. α,α'-Dipyridyl ketone (0.6 g.) and 0.7 g. I in 25 cc. C6H6 refluxed 3 hrs. yielded XII, m. 164°. Fluorenone did not react with I in refluxing C6H6-MeOH.

L9 ANSWER 61 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Application of thin-layer chromatography for separation and identification of antibiotics

AB Fifty kinds of known antibiotics (10 γ) were separated by thin-layer chromatography and detected by 10% KMnO4 and 0.2% bromophenol blue or by specific color reactions. The solvents were: for macrolide, BuOH-AcOH-H2O (3:1:1) (solvent 1), EtOH-concentrated NH4OH-H2O (8:1:1) (solvent 2), or EtOH-H2O (4:1) (solvent 3); for basic antibiotics, the upper layer of CHCl3-MeOH-17% NH4OH (2:1:1) or PrOH-pyridine-AcOH-H2O (15:10:3:12); for peptide or antifungal antibiotics, solvent 1; for polyene, solvent 2 or 3, or EtOAc-MeOH (100: 15); for nucleotides, EtOAc-MeOH (2:1). Rf values are given.

L9 ANSWER 62 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Azomethine derivatives of 2-**pyrrolecarboxaldehydes.** III. Condensation products of **pyrrole**-2-carboxaldehydes with amino acids

AB cf. CA 54, 14227g. **Pyrrole**-2-carboxaldehyde (I) (0.19 g.) and 0.17 g. alanine were dissolved in 2 ml. 50% EtOH, 0.165 g. (AcO)Ba in 1 ml. H2O2 added, heated on a H2O bath, and cooled to yield Ba salt of N-(2-**pyrrolemethylene**)alanine (II), m. 243°. Similarly was prepared N-(2-**pyrrolemethylene**)valine (III), m. 205°. Glycine (0.075 g.) and 0.3 g. brucine (IV) were dissolved in 8 ml. 20% EtOH, 0.095 g. I added, heated, and concentrated to small volume to give on cooling IV salt of N-(2-**pyrrolemethylene**)glycine, m. 100°. Similarly were prepared the following IV salts (acid, m.p. given): II, 102°; N-(2-**pyrrolemethylene**)phenylalanine, 164°; III, 182°.

L9 ANSWER 63 OF 63 CAPLUS COPYRIGHT 2004 ACS on STN

TI Inhibition by antibiotics of the growth of bacterial and yeast protoplasts
AB The characteristics and requirements for growth of bacterial (Streptococcus faecalis) and yeast (Saccharomyces cerevisiae) protoplasts were established and the effect of a variety of antibacterial and antifungal antibiotics determined A clear differentiation was obtained between such inhibitors of bacterial cell wall synthesis as penicillin and cycloserine, which did not prevent protoplast growth, and all others, antibacterial and antifungal, which inhibited protoplasts and intact organisms at the same range of concentration Novobiocin, previously reported to inhibit bacterial wall synthesis, was also effective against a reaction(s) essential to the growth of S. faecalis protoplasts. The antibacterial action of streptomycin, neomycin, and kanamycin was essentially eliminated by the high salt concentration needed to maintain the protoplasts. Removal of the cell wall did not significantly increase antibiotic susceptibility of a resistant species. Protoplasts of Bacillus megaterium were insensitive to the antifungal agent, nystatin, and did not bind it to any detectable degree. Thus, the yeast or bacterial cell wall does not appear to play a major role in determining relative antibiotic susceptibility by masking internal sensitive target sites. A variety of antifungal antibiotics tested on the growth of log-phase yeast cells failed to produce osmotically fragile forms.

=> s L9 and epox?
1 FILES SEARCHED...
L10 19 L9 AND EPOX?

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L10 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Cycloaddition reaction of **epoxides** with various alkenes under microwave irradiation
AB The reactivity of gem-dicyano **epoxides** with various alkenes is studies in solvent free conditions, and in homogeneous solution, under microwave irradiation Reactants included 3-phenyl-2,2-**oxiranedicarbonitrile**, 3-(4-methoxyphenyl)-2,2-**oxiranedicarbonitrile**, 3-(4-chlorophenyl)-2,2-**oxiranedicarbonitrile**, 3-(4-nitrophenyl)-2,2-**oxiranedicarbonitrile.** Microwave heating of these substrates in solvent, yields carbonyl ylides which give 1-3-dipolar cycloaddn. For example, the reaction of 3-phenyl-2,2-**oxiranedicarbonitrile** with (2E)-2-butenedioic acid di-Me ester gave 2,2-dicyanotetrahydro-5-phenyl-3,4-furandicarboxylic acid di-Me ester. The reaction of 3-phenyl-2,2-**oxiranedicarbonitrile** with 1-phenyl-1H-**pyrrole**-2,5-**dione** gave hexahydro-4,6-dioxo-3,5-diphenylfuro[3,4-c] **pyrrole**-1,1-dicarbonitrile.

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L10 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
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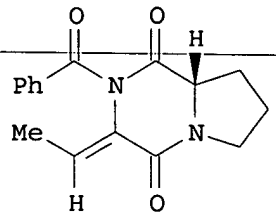
L10 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Stereoselective **epoxidation** and bromoalkoxylation with 3-ylidenepyrazine-2,5-**diones**
GI



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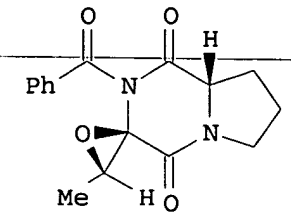

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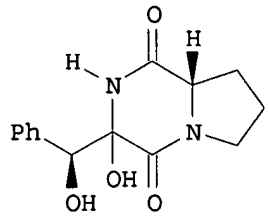

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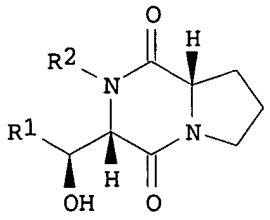


IV

AB 3-Ylidenepyrazine-2,5-**diones**, e.g., I, were stereoselectively **epoxidized** by dimethyldioxirane giving access to spirooxiranes, e.g., II, and diols, e.g., III. Bromohydroxylation and bromoalkoxylation of 3-ylidenepyrazine-2,5-**diones** produced high yields of optically active 3-(1-bromoalkyl)pyrazine-2,5-**diones** with a 3-hydroxy or 3-alkoxy function, resp. Whereas direct hydrogenation of **epoxides** afforded epimeric mixts. of 3-(1-hydroxyalkyl)pyrazine-2,5-**diones**, the highly stereoselective transformation into IV (R1 = Me, i-Pr, R2 = PhCO; R1 = Ph, R2 = H)was possible by primary acid cleavage of the **oxirane** ring followed by hydrogenation of the resulting keto-enol mixts.

L10 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of substituted oxazolidinones for combinational therapy in the treatment and/or prophylaxis of thromboembolic diseases
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to combinations of (A) oxazolidinones I [R1 = 5-X-2-thienyl (X = Cl, Br, Me, CF3); R2 = DA; A = phenylene; D = 5- or 6-membered heterocyclic ring containing S, N or O; R4 - R8 = H], or their pharmaceutically acceptable salts, hydrates, prodrugs or their mixts. and (B) other pharmaceutically active ingredients; to a method for producing said combinations; and to the use thereof as medicaments, in particular for the treatment and/or prophylaxis of thrombo-embolic diseases. Thus, the claimed oxazolone II was prepared from **epoxide** III via

epoxide ring opening with aniline derivative IV, cyclization with carbonyldiimidazole, and N-acylation with 5-chlorothiophene-2-sulfonyl chloride. II was tested for antithrombotic activity in the arteriovenous shunt model (Rat) after [ED50 = 3 mg/kg (p.o.); IC50 = 0.7 nM]; II had a synergistic effect when used in combination with clopidogrel.

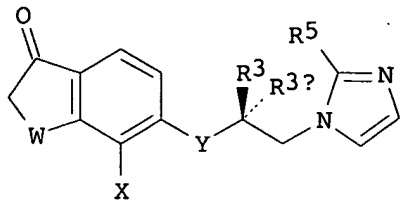
L10 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Isomerization of cyclic ethers having a carbonyl functional group: new entries into different heterocyclic compounds
AB **Oxiranes** (**epoxides**) and oxetanes having a carbonyl functional group are chemoselectively isomerized to different heterocyclic compds. via Lewis acid-promoted 1,6- and 1,7-intramol. nucleophilic attacks of the carbonyl oxygen on the electron-deficient carbon neighboring the oxonium oxygen: for example, cyclic imides to bicyclic acetals, esters to bicyclic ortho esters, sec-amides to 4,5-dihydrooxazole or 5,6-dihydro-4H-1,3-oxazines, and tert-amides to bicyclic acetals or azetidines. The intramol. attack of a 1,5-positioned carbonyl oxygen predominantly results in a propagating-end isomerization polymerization On the other hand, cyclic ethers having a 1,8- or farther positioned carbonyl group undergo conventional ring-opening polymerization A THF (oxolane) ring does not open, even with a 1,6-positioned carbonyl group.

L10 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI New aryl-, quinolyl-, and other heterocyclyl-containing amino alcohol derivatives useful as β3 adrenergic receptor agonists
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to compds. I [wherein: X1 = bond or OCH2; X2 = (CH2)1-2; X3 = bond, O, or NH; R1 = (un)substituted Ph, indolyl, or carbazolyl [substituents = 1 or 2 of OH, halo, NO2, amino, formyl, (lower)alkylsulfonylamino, aryl(lower)alkoxy, and hydroxy(lower)alkyl]; R2 = H or aryl(lower)alkyl; R3 = H or hydroxy(lower)alkyl; R4 = (un)substituted aryl, 4-quinolyl, phthalazinyl, quinazolinyl, cinnolinyl, or naphthyridinyl; with provisos], or their pharmaceutically acceptable salts. The compds. are β3 adrenergic receptor agonists, and therefore have gut sympathomimetic, antiulcer, anti-pancreatitis, lipolytic, and smooth muscle relaxant activities. In particular, I and salts are useful for the prophylactic and/or the therapeutic treatment of pollakiuria or urinary incontinence. Sixty precursor prepns. and 63 invention examples, including well over 200 invention compds., are provided. For example, the structure of claimed compound II is typical. Another invention compound, phthalazine derivative III, was prepared from 4-((2S)-2-amino-3-hydroxypropyl)phenol HCl, benzaldehyde, (2S)-3-phenoxy-1,2-**epoxypropane**, and 1-chlorophthalazine, in 4 steps. III at 0.32 mg/kg (intraduodenal) in beagle dogs gave 35.9% inhibition of carbachol-induced increase in intravesical pressure.

L10 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of 5-substituted tetralones as inhibitors of ras farnesyl transferase for treatment of proliferative diseases
GI



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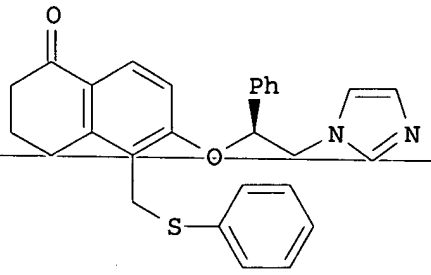


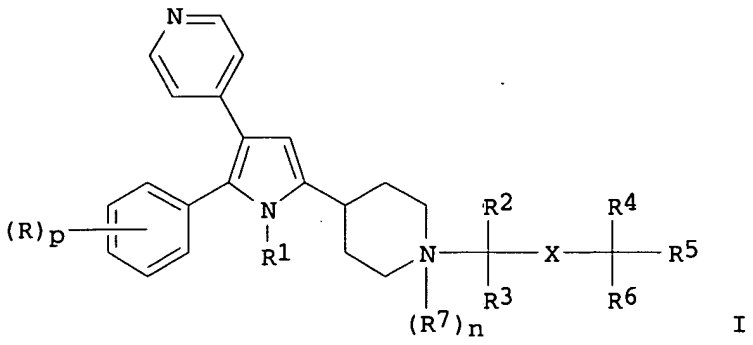
II

AB Title compds. I [wherein W = CH2 or CH2CH2; R3 = H, alkyl, or (un)substituted Ph; R3a = H or alkyl; provided that R3 and R3a cannot both be H and that when R3 = (un)substituted Ph, then R3a = H; X = halo, NH2, alkyl, alkenyl, heteroaryl, CH2OR6, CH2NR6R6a, CH2SR6, CH2CH2CO2R6, or (un)substituted aryl, or (hetero)arylalkyl; R6 = H, (cyclo)alkyl, alkenyl, benzyl, or (un)substituted Ph; R6a = H or alkyl; Y = O or S; R5 = H, alkyl, or NH2; and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof] were prepared and formulated as farnesyl transferase enzyme inhibitors. For example, coupling of 5-chloromethyl-6-hydroxy-2,3,4-trihydronaphthalen-1-one with thiophenol using diisopropylamine in THF (58%), followed by addition of (R)-2-imidazol-1-yl-1-phenylethanol in the presence of PPh3 and di-Et azodicarboxylate in THF (31%), gave II. The latter inhibited farnesyl protein transferase (FPT) with IC50 of 0.3 nM. I are useful for treating and preventing uncontrolled or abnormal proliferation of tissues, such as cancer, atherosclerosis, restenosis, and psoriasis (no data).

L10 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

TI Aliphatic hydroxy substituted piperidyl diaryl **pyrrole** derivatives as antiprotozoal agents

GI



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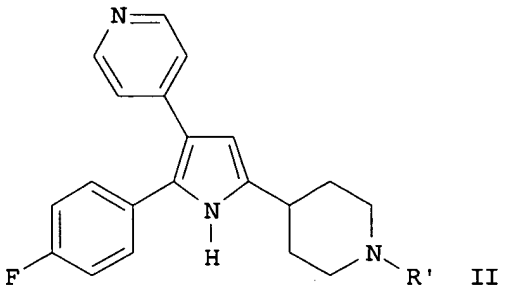
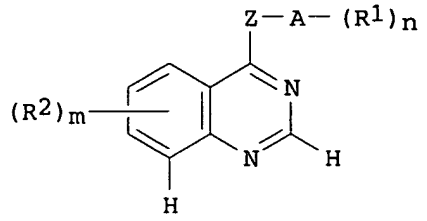


II

AB Trisubstituted **pyrroles** I are antiprotozoal agents (no data), useful in the treatment and prevention of protozoal diseases in human and animals, including the control of coccidiosis in poultry [wherein: n = 0-1; p = 1-3; X = bond, (un)substituted (CH2)1-3, cycloalkylene, cycloalkylidene; R = halo; R1 = H or alkyl; R2, R3 = H, (un)substituted alkyl, alkenyl, alkynyl, (un)substituted Ph or CH2Ph, CO2H or derivs.; or R2R3 = O; R4 = OH or SH or their derivs.; R5, R6 = H, alk(en/yn)yl, cycloalkyl(alkyl), (hetero)aryl(alkyl), heterocyclyl(alkyl), CO2H or OH or derivs.; or R4R5 or R5R6 forms 3- to 7-membered hetero ring; or R4R6 = O; or R2R4 or R2R5 forms 4- to 7-membered carbo or hetero ring; R7 = O, Me; and physiol. acceptable salts]. Approx. 200 compds. were prepared For instance, 4-picoline was lithiated and condensed with 4-FC6H4CONMeOMe, and the resulting ketone was deprotonated and coupled with 4-(2-iodoacetyl)-1-(benzyloxycarbonyl)piperidine to give a 1,4-diketone. Cyclization of this with ammonium acetate and deprotection gave **pyrrole** intermediate II [R' = H], which was N-alkylated by (R)-glycidyl Me ether to give title compound II [R' = (R)-CH2CH(OH)CH2OMe].

L10 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of quinazoline derivatives as angiogenesis inhibitors
GI



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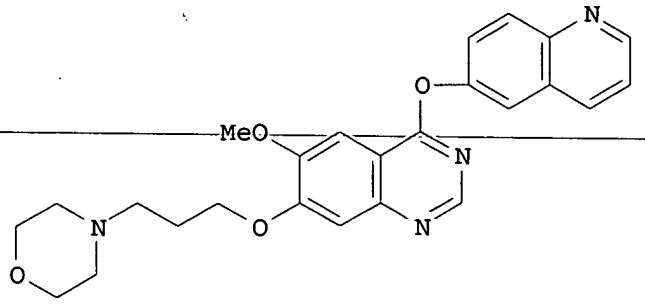
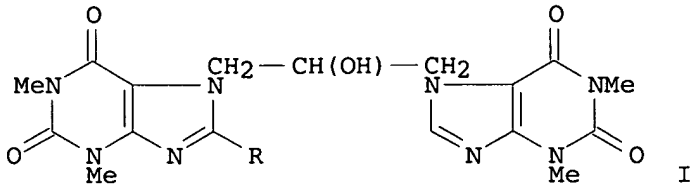


II

AB The title compds. (I) [wherein A = an 8-, 9-, 10-, 12- or 13-membered bicyclic or tricyclic ring optionally containing 1-3 O, N, and/or S heteroatoms; Z = O, NH, S, CH2, or a bond; n = 0-5; m = 0-3; R2 = H, OH, halo, CN, NO2, CF3, alkyl(sulfanyl), alkoxy, NR3N4, or R5X1; R3 and R4 = independently H or alkyl; X1 = a bond, O, CH2, OC(O), CO, S, SO, SO2, NR6CO, CONR7, SO2R8, NR9SO2, or NR10; R5 = H or (un)substituted alkyl, alkenyl, alkynyl, or heterocyclyl, etc.; R6-R10 = independently H or (alkoxy)alkyl] were prepared for use in the production of an antiangiogenic and/or vascular permeability reducing effect in warm-blooded animals. For instance, II was synthesized in a 9-step sequence starting with the cyclization of 2-amino-4-benzyloxy-5-methoxybenzamide using Gold's reagent in dioxane to form 7-benzyloxy-6-methoxy-3,4-dihydroquinazolin-4-one (84%). I and the pharmaceutically acceptable salts thereof inhibit the effects of VEGF, a property of value in the treatment of a number of disease states including cancer and rheumatoid arthritis (no data).

L10 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Studies on the methylxanthine series. IX. Synthesis and physicochemical characterization of 1-(8-substituted 1,3-dimethylxanthin-7-yl)-3-(1,3-dimethylxanthin-7-yl)-2-hydroxypropane derivatives
GI



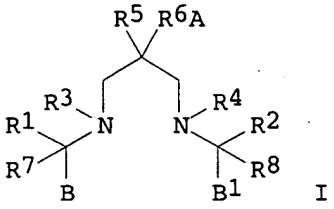
I

AB Title compds. I (R = H, Br, NO2, 1-**pyrrolidinyl**, piperidino, morpholino, etc.) were prepared by reaction of 8-substituted 1,3-dimethylxanthines with 7-(**epoxypropyl**)-1,3-dimethylxanthine.

L10 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Detection and identification of volatile substances by headspace capillary gas chromatography to aid the diagnosis of acute poisoning
AB Headspace gas chromatog. with split flame-ionization-electron-capture

detection is a simple method of screening for a wide range of volatile substances in biol. fluids. A 60 m x 0.53 mm i.d. thick-film (5 μm) fused-silica capillary coated with SPB-1 (Supelchem) with split flame-ionization-electron-capture detection provides a valuable alternative to packed columns in this work. Most commonly abused compds., including many with very low b.ps. such as bromochlorodifluoromethane, butane, di-Me ether, FC 11, FC 12, isobutane, and propane, can be retained and differentiated at an initial column temperature of 40° followed by programming to 200°. The total anal. time is 26 min. Retention and detector response date were generated for 244 compds. Good peak shapes are obtained for polar analytes such as ethanol and injections of up to 0.03 cm3 of headspace can be performed with no discernable loss of efficiency. The sensitivity is thus at least as good as that attainable with packed columns. Of the commonly encountered compds., only isobutane-methanol and paraldehyde-toluene are at all difficult to differentiate. Quant. measurements can be performed either isothermally or by using the temperature program.

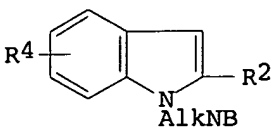
L10 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of propanediamine derivatives as ligands for radioactive isotopes, their metal complexes, and their use in diagnosis and therapy
GI



I

AB The title ligands [I; R1, R2, R5 = H, (HO-substituted) C1-6 alkyl; R3, R4 = H, (amino)C1-6 alkyl, HO2CCH2, (C1-6 alkoxycarbonyl)methyl or -benzyl; R6 = C1-6 alkylene; R7, R8 = H, C1-6 alkyl; B, B1 = Ph, 2-HSC6H4, naphthyl, thienyl, **pyrrolyl**, all optionally substituted by 1-3 HO), CH(NO)R9; R9 = C1-6 alkyl; R1R9, R2R9 can form a 5- or 6-membered ring with (CH2)3 or (CH2)4; A = functional group Z, a compound T bound to R6 via Z and capable of accumulating itself in lesions or specific tissues, e.g. an enzyme, amino acid, saccharide, a growth factor, especially a monoclonal antibody or its fragments, biotin, and misonidazole; Z = amino, carboxy, HO, **oxiranyl**, aminophenyl, C2-6 alkenyl, etc.], useful in tumor diagnosis and therapy, were prepared Condensation of 4-O2NC6H4CH(CH2NH2)2 [preparation from CH2(CO2Et)2 and 4-O2NC6H4CH2Br given] with 2-chloro-2-methyl-3-nitrosobutane gave 27% 6-(4'-nitrobenzyl)-3,3,9,9-tetramethyl-4,8-diazaundecane-2,10-**dione** dioxime. This was reduced (26%) to its 4'-aminobenzyl analog, chelated by Cu(OAc)2 (45%), the Cu-chelate coupled (75%) at position 4' with biotin N-hydroxysuccinimide ester, the resulting biotin conjugate decomplexed (41%) by KCN, and the ligand recomplexed with a radioactive tracer: technetium-99m (200 μCi). A rat left hind leg muscle was injected with 20 μL of a com. streptavidin-Sepharose conjugate and, 30 min later, with 5 μg (i.v.) of the latter chelate (purity >90%). After 4 h, the radioactivity in the left hind leg was 14-fold higher than in the right hind leg, and it contained 1.4% of the total of the applied dosis/g muscle.

L10 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Preparation of 1-(aminoalkyl)indoles useful as analgesic agents or as intermediates and their production processes
GI



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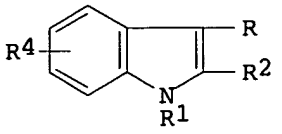

II

AB Title compds. I [R2 = H, alkyl, Cl, (un)substituted Ph, (un)substituted PhCH2; R4 = H, 1 or 2 substituents such as alkyl, HO, alkoxy, halo in 4-, 5-, 6-, or 7 position; alk = (un)substituted α,ω-alkylene (CH2)n; n = 2-6; NB = N3, H2N, alkylamino, hydroxyalkylamino, morpholino, thiomorpholino, piperidino, **pyrrolidino**, azetidino, **pyrrolidino**, 1-piperazinyl, hexahydro-4H-1,4-diazepinyl, their oxides, etc.] or an acid addition salt thereof, useful as analgesics (no data) are prepared II (R = R3CZ, R3COCH:CH, R3CO; R3 = cyclohexyl, heterocycylphenyl, aminomethylphenyl, (un)substituted styryl, biphenyl, (un)substituted naphthyl, heterocyclyl, etc.; CZ = CO, HONC; R1 = H, BNAlk, BNCH2CH(OH)CH2] were also prepared and found to possess analgesic, antiinflammatory and antirheumatic activities. II [R = 3-(O2N)C6H4CO; R1 = 2-morpholinoethyl; R2 = Me; R4 = H] in EtOAc and AcOH was reduced with H over Pt oxide to give 83% II [R = 3-(H2N)C6H4CO; R4 = morphoninoethyl; R2 = Me; R4 = H] (III). III, on oral administration, showed and ED50 in acetylcholine-induced abdominal constriction and antibradykinin test of 16 and 53 mg, resp., and on the rat paw flexion test 0.12% at 100 mg/kg.

L10 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI The structural basis of the mutagenicity of chemicals in Salmonella typhimurium: The Gene-Tox data base
AB The CASE (Computer Automated Structure Evaluation) structure-activity methodol. has been applied to a Gene-Tox derived Salmonella mutagenicity data base consisting of 808 chems. Based upon qual. structural features, CASE identified 29 activating and 3 inactivating structural determinants which correctly predicted the probability of carcinogenicity of 93.7% of the known mutagens and nonmutagens in the data base (sensitivity = 0.998, and specificity = 0.704). Addnl., based upon a qual. structure-activity anal., CASE's performance was even better, leading to a sensitivity of 0.981 and a specificity of 1.000. Using the structural determinants identified in this data base, CASE gave excellent predictions of the mutagenicity of chems. not included in the data base. The identified biophores and biophobes can also be used to investigate the structural basis of the mutagenicity of various chemical classes.

L10 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Arylimide-**epoxy** resin composites
GI For diagram(s), see printed CA Issue.
AB Resin compns. suitable for curing to tough thermally stable thermoset composites having high glass transition temps., Tg and high modulus plateaus above Tg contain 5-95% arylimide (I; q = 6-8; s = 1-2) (prepared from chlorinated terphenyl-sodium aminophenolate polyamines and maleic anhydride) and 95-5% **epoxy** resin. Thus, 11.05 lb 49.7% NaOH was added to a refluxing mixture containing 15.14 lb p-aminophenol [123-30-8], 38.19 lb Aroclor 5460 [11126-42-4], 8.0 gal xylene, and 9.0 gal N-methylpyrrolidinone, xylene was distilled until pot temperature 165° was attained, and 13.61 g maleic anhydride [108-31-6] was added. A mixture of 70 g arylimide product and 30 g **epoxylated** novolak with **epoxy** equivalent 180-220 g/g-mole **oxirane** oxygen was melt blended at 160°, B-staged for 2 min at 265°, and compression molded for 3 min at 265°. The thermoset composite had Tg 35,000 psi, shear modulus 1.1 + 1010 dynes/cm2, and shear modulus above Tg 8.5 + 108 dynes/cm2.

L10 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN

TI Resin laminates
AB Substrates were coated with mixts. of bismaleimides 30-60, **epoxy** compds. 65-25, and cyanuric acid [108-80-5] 5-15% and laminated by heating under pressure. Thus, Epikote 1007 [25068-38-6] 19, an alkyl-modified bisphenol **epoxy** resin 35, and isocyanuric acid [108-80-5] 11 parts were dissolved in DMF to give a 50% solution, stirred at 150-5° for .apprx.3 hr, mixed with 35 parts N,N'-(methylenedi-p-phenylene)bismaleimide [13676-54-5], diluted with DMF to 50%, coated on glass cloths treated with γ-aminopropyltriethoxysilane, and dried at 160° for 5 min to prepare prepregs which were pressed at 180° (50 kg/cm2) to form a laminate.

L10 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Heat-hardenable compositions
AB Reaction of **epoxy** resins with bis(4-aminophenyl)methane [101-77-9] and 4-maleimido-4'-acetamidodiphenylmethane [53184-84-2], 4,4'-diphenylmethanebismaleimide [13676-54-5] or 4-maleimido-4'-acetoxysuccinimidodiphenylmethane [53184-85-3] gave heat hardenable moldings.

L10 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI 10α-Methyl-9β-hormonal steroids
AB 4,7,22-Lumistatrien-3-one (125 g.) in 2.2 l. iso-PrOH previously saturated with dry HCl, dry HCl passed through the solution for 0.5 hr., and worked up gave 80.5 g. lumista-4,6,22-trien-3-one (I), m. 101-2° (ligroine), [α]25D -632° (all rotations in CHCl3 unless otherwise mentioned). I (3 g.) in 300 ml. Et2O added to 450 ml. liquid NH3, treated with 420 mg. Li in NH3 and the product chromatographed on Al2O3 gave 2.43 g. lumista-4,22-dien-3-one (II), m. 122-4° (Me2CO), [α]20D -125°. II(20g.)in 750 ml. CH2Cl2 and 5.75 ml. C5H5N ozonized 4.5 hrs. at -80 gave 10.1 g. 3-oxo retrobisnor-4-cholen-22-al (III), m. 122-30° (ligroine), [α]23D -144°. III (450 mg.) in 15 ml. CHCl3 and 25 ml. AcOH oxidized 16 hrs. at 30° with 200 mg. CrO3 and 0.2 ml. H2O gave 340 mg. 3-oxoretrobisnor-4-cholenic acid (IV), m. 202-4° (Et2O). Alternatively a solution of 450 mg. of an ozonide of II in 25 ml. CH2Cl2 left overnight at 30° with 200 mg. CrO3 in 25 ml. AcOH gave 150 mg. IV. III (300 mg.), 0.11 ml. piperidine, and 1 to 5 mg. p-MeCoH4SO3H refluxed 3 hrs. in 5 ml. dry C6H6 gave 185 mg. 22-(N-piperidyl)retrobisnorchola-4,20(22)dien-3-one (V), m. 94-6° (MeOH). Other samples of V m. 114-15° (probably due to cis-trans isomerism). Alternatively 10 g. III refluxed 3 hrs. in 180 ml. C6H6 with 3.8 ml. piperidine and 30 mg. p-MeC6H4SO3H gave 9.3 g. V. III (1 g.) refluxed with 0.5 g. fused NaOAc and 50 ml. Ac2O gave 22-acetoxyretrobisnorchola-4,20(22)-dien-3-one (VI). V (300 mg.) in 4.5 ml. C6H6 added in 45 min. at -5° to +5° to 453 mg. Na2Cr2O7.2H2O in 4.5 ml. AcOH and 3 ml. C6H6 and the product worked up gave 150 mg. retroprogesterone (VII), m. 163-4° (CH2Cl2-ligroine), [α]20D - 62°. III treated with NaOAc in Ac2O gave VI and VI ozonized, decomposed, and hydrolyzed gave VII. VII (10 g.) in 79 ml. C6H6 stirred 1.5 hrs. with NaOMe in diethyl oxalate and some C6H6 gave 10.8 g. Na enolate of 21-ethoxyoxalylretroprogesterone (VIII). VIII in 150 ml. MeOH treated 40 min. at -20 with 5.9 g. iodine in 210 ml. MeOH, mixture stirred 1.5 hrs., and the iodine compound decomposed with NaOMe solution gave 5.55 g. 21-iodoretroprogesterone (IX). IX (5.55 g.) refluxed 18 hrs. in 200 ml. Me2CO with 12 g. KOAc and chromatographed on Al2O3 gave 335 mg. retrodeoxycorticosterone acetate, m. 165-8° (alc.). V (9.6 g.) in 475 ml. CH2Cl2 treated dropwise at -55°with 4.08 g. Br in 50 ml. CH2Cl2, the dibromo compound stirred 2 hrs. at 20°, the 20-bromo derivative heated 1 hr. at 70° with 70 ml. C5H5N, then 0.5 hr. at 100°, and worked up gave 6 g. 3-oxoretrobisnorchol-4,17(20)-dien-22-al (X), m. 155-9° (Me2CO-alc.), [α]23D -138°. III (7.7 g.) in 100 ml. CCl4 treated with 48 ml. Br solution in CCl4 (0.515 mole/ml.) and 3 g. CaCO3 and then treated with C5H5N gave 7.15 g. X. X (5 g.) suspended with 8 g. NaCN in 50 ml. MeOH at -20°, left 2 hrs. at 20°with 7.1 ml. AcOH, then 40 hrs. at 5°, and worked up gave

the 22-HCN addition product of X which treated at -80° with O3 gave 1.48 g. retroandrost-4-en-3,17-**dione** (XI), m. 154-6° (alc.). XI (3.03 g.) in 25 ml. C6H6 and 25 ml. Et2O left 16 hrs. with 1.61 g. K in liquid NH3 which had been treated with CH.tplbond.CH gave 1.95 g. 17α-ethynylretrotestosterone (XIa), m. 195-6° (hexane), [α]20D -219. 3-Oxoretrobisnorchola-4,6-dien-22-al (XII) (3.5 g.) in 50 ml. C6H6 refluxed 2.5 hrs. with 1.27 ml. piperidine and 20 mg. p-MeC6H4SO3H gave 2.1 g. 22-(N-piperidyl)retrobisnorchola-4,6,20(22)-trien-3-one (XIII), m. 135-6° (Me2CO). XIII oxidized with Na2Cr2O7 in AcOH gave 6-dehydroretroprogesterone (XIV), m. 168-9° (Me2CO). Lumisterone (3.95 g.) in 150 ml. CH2Cl2 and 0.81 ml. C5H5N treated with O3 gave 3.11 g. 3-oxoretrobisnorchola-4,7-dien-22-al (XV), m. 196-200° (CH2Cl2-Me2CO). XV treated with piperidine and then oxidized with Na2Cr2O7 gave 7-dehydroretroprogesterone (XVI). By isomerization of the 3-oxo-4,7-dehydro system of XVI with dry HCl XIV was obtained. VII (7.5 g.) in 500 ml. tert=BuOH refluxed 5 hrs. with 12.75 g. chloranil and the product chromatographed on Al2O3 gave XIV. I (3.95 g.) ozonized as described above gave 3.08 g. XII, m. 153-5° (Me2CO). 3-Oxoretrobisnorchol-4,20(22) dien-22-al (0.978 g.) in 10 ml. C6H6 kept 4 hrs. at 0° with 1.2 g. monoperphthalic acid in 25.5 ml. EtOAc gave 0.88 g. 17(20)**epoxy**-20-formyloxyretropregn-4-en-3-one (XVII). Hydrolysis of XVII with 2N NaOH gave 17α-hydroxyretroprogesterone (XVIII), m. 222-5° (alc.). XIII (6.5 g.) treated with Br and then with C5H5N gave 2.41 g. retrobisnorchola-4,6,17(20)-trien-3-one-22-al (XIX), m. 217-19° (Me2CO). XIX (15 g.) in 150 ml. EtOAc and 150 ml. C6H6 treated with 20.2 g. monoperphthalic acid in 450 ml. EtOAc and left 16 hrs. gave 16.4 g. resinous **epoxy**-20-formyloxy compound which treated 1.5 hrs. at 30° with 2N NaOH gave 5.69 g. 6-dehydro-17α-hydroxyretroprogesterone (XX). XIX (3.7 g.) treated as above with 5.9 g. NaCN and MeOH followed by ozonization gave 1.2 g. retroandrosta-4,6-diene-3,17-**dione**, m. 189-90° (Me2CO). XVIII (220 mg.) and 220 mg. p-MeC6H4SO3H in 15 ml. AcOH kept 18 hrs. at room temperature gave 130 mg. 3,17-diacetate of XVIII, m. 217-18° (CH2Cl2-MeOH). XVIII (0.5 g.) similarly treated but in less Ac2O and the product fractionally crystallized gave 260 mg. 17α-acetoxyretroprogesterone, m. 171-3° (MeOH). XVIII (900 mg.) treated with caproic anhydride and p-MeC6H4SO3H, then with 0.3 ml. concentrated HCl in 20 ml. alc., and the product chromatographed gave 67 mg. 17-caproate of XVIII, m. 50-3° (hexane). Many esters of XVIII were similarly preparing XVIII (0.495 g.) in tert-BuOH treated with chloranil gave 50 mg. XX, m. 242-5° (alc.-hexane). 6-Dehydro-17α-acetoxyretroprogesterone, m. 181-3°, was similarly prepared Retroprogesterone hydroxylated with Rhizopus nigricans gave a hydroxyretroprogesterone, m. 217-18°, and 17α,21-dihydroxyretroprogesterone (XXa) incubated with Aspergillus ochraceusgave retrohydrocortisone, m. 269° (decomposition). XIa (1.88 g.) in 50 ml. C5H5N hydrogenated over 2 g. Pd-CaCO3 gave 1.17 g. 17α-vinylretrotestosterone, m. 143.5-5.5° (Me2CO-hexane). VII (5 g.) in 250 ml. C6H6 refluxed 7 hrs. with 4 g. dichlorodicyanobenzoquinone and the product chromatographed on silica gel gave 2.14 g. 1-dehydroretroprogesterone, m. 154-5.5° (Me2CO-hexane). XIV (2.5 g.) gave 208 mg. dioxime, m. 279-82° (tetrahydrofuran-ligroine). I (75 g.) and 55 ml. HCO2Et in 1.2 l. C6H6 kept 3 days at room temperature with 16.5 g. NaH and the Na salt converted to the free alc. gave 2-hydroxymethylenelumista-4,6,22-trien-3-one (XXI) as the hydrate, m. 119-22°, anhydrous form m. 122-3.5°. Similarly, II gave 2-hydroxymethylenelumista-4,22-dien-3-one (XXII), m. 134-5°. XXI (108 g. of Na salt) in 3.2 l. alc. treated 3.5 to 4.5 hrs. at 10° with perchloryl fluoride gave 71 g. 2-fluorolumista-4,6,22-trien-3-one (XXIII), m. 158-60° (MeOH), [α]27D -635° (alc.). XXII similarly gave 2-fluorolumista-4,22-dien-3-one. XXIII (30.5 g.) in 610 ml. CH2Cl2 and 10 ml. C5H5N treated with O3 at -80° gave 16.6 g. 2-fluororetrobisnorchola-4,6-dien-3-on-22-al (XXIV), m. 183-5° (CH2Cl2-Et2O). XXIV (2.08 g.) similarly treated with piperidine and p-MeC6H4SO3H gave 2-fluoro-22-(N-piperidyl)-retrobisnorchola-4,6,20(22)-

trien-3-one, which with CrO3 gave 2-fluoro-6-dehydroretroprogesterone, m. 153-4° (alc.). Retropregnane-3,20-**dione** (XXV) (300 mg.) in alc. treated 3 hrs. at -20° with 36.6 mg. CaCl2.2H2O and 16.3 mg. NaBH4 gave retropregnan-3-ol-20-one, m. 167-71° (alc.-E+2O). VII (2.826 g.) in 150 ml. dioxane shaken with excess H over 0.3 g. 10% Pd-C in the presence of 0.6 g. KOH in 9 ml. MeOH gave XXV, m. 115-16° (E+2O-hexane). XIV (5 g.), 7.5 g. chloranil, and 25 g. CaCO3 refluxed 3 hrs. with 170 ml. isoamyl alc. and chromatography of the product gave XIV and 150 mg. 1,6-bisdehydroretroprogesterone (XXVI). XIV (5 g.) and 5.1 g. dihydroquinone in 250 ml. C6H6 refluxed 6 hrs. gave 1.52 g. XXVI, m. 143-3.5° (Me2CO-hexane). VII enol acetate (7.5 g.) and dioxane treated at room temperature with perchloryl fluoride gave 185 mg. 6α-fluororetroprogesterone (XXVII), m. 150-1° (Me2CO-hexane), 1.16 g. 6β-fluororetroprogesterone (XXVIII), m. 163-5° (MeOH), and 77 mg. 6-hydroxyretroprogesterone, m. 220-2° (Me2CO). XXVII (50 mg.) in 10 ml. CHCl3 treated 1 hr. with passage of dry HCl gave XXVIII. XVIII (1 g.) in 15 ml. tetrahydrofuran and 2.5 ml. MeOH treated at -4° to 0° with 1.5 g. iodine and the product refluxed with KOAc in Me2CO gave 772 mg. 17α,21-dihydroxyretroprogesterone 21-acetate (XXIX), m. 218-238° (decomposition) (Me2CO). XX (1 g.) in 15 ml. tetrahydrofuran and 2.5 ml. MeOH similarly treated with iodine and the product refluxed with KOAc in Me2CO gave 915 mg. 6-dehydro-17α,21-dihydroxyretroprogesterone 21-acetate, m. 238.5-44° and 257-9° (decomposition). XXIX (1.2 g.) in 30 ml. MeOH stirred 2 hrs. at 24° with 216 mg. K2CO3 in 6 ml. H2O gave 897.5 mg. XXa. XIa (3.12 g.) in 250 ml. dioxane reduced with H over PdCaCO3 and the product chromatographed on silica gel gave 300 mg. 17α-ethyl-5-retroandrostan-17-ol-3-one (A isomer), m. 125-6.5° (Et2O-petr. ether) and 828 mg. B isomer, m. 125-6.5°. VII was converted to its 3-enol acetate, m. 90-2° (MeOH). Retroandrosta-4,6-diene-3,17-**dione** (2.35 g.) in 70 ml. 2:1 mixture C6H6-Et2O stirred 0.5 hr. at -80° with 1.28 g. K in 50 ml. liquid NH3 previously treated with CH.tplbond.CH gave 6-dehydro-17α-ethynylretrotestosterone, m. 205-7° (Me2CO-hexane). IX (6.6 g.) in 200 ml. MeCN and 5.72 g. AgF stirred 25 hrs. at 45° gave 21-fluororetroprogesterone, m. 173-5° (alc.-Me2CO). XIV (10 g.) in 70 ml. C6H6 stirred 1.5 hrs. with 8.5 ml. (CO2Et)2 and 10.5 ml. of a 3.45N NaOMe solution in MeOH, 70 ml. C6H6, and 3.2 ml. alc. gave 12.2 g. Na enolate of 21-ethoxyoxalyl-6-dehydroretroprogesterone (XXX). XXX in 170 ml. MeOH treated at -25° with 7.2 g. iodine gave 12-iodo-6-dehydroretroprogesterone (XXXI). XXXI refluxed 5 hrs. with KOAc in Me2CO, H2O, and AcOH gave 6-dehydro-21-acetoxyretroprogesterone, m. 194.5-7.5°. XIV (937 mg.) in 125 ml. CCl4 treated in 50 min. with 0.5 g. Br in 10 ml. CCl4 gave 4-bromo-6-dehydroretroprogesterone m. 121-2° (MeOH) (decomposition). XIV with Cl similarly afforded 4-chloro-6-dehydroretroprogesterone, m. 185-6°. 6-Chlororetroprogesterone (XXXII) (700 mg.) and 1 g. chloranil refluxed 30 hrs. in 100 ml. tert-BuOH gave 6-chloro-6-dehydroretroprogesterone, m. 165-6° (alc.). 3-Acetoxyretropregna-3,5-dien-20-one (XXXIII) (1.85 g.) in 30 ml. Et2O, 4 g. KOAc, 60 ml. 85% AcOH treated with 375 mg. Cl in 9.4 ml. AcOH gave XXXII, m. 197-9.5° (EtOAc), and 3,6,20-trioxoretropregnane, m. 201-3°. 6-Bromoretroprogesterone was similarly prepared, m. 138-40° (decomposition). XIV (5 g.) reduced with NaBH4 in alkali gave retropregna-4,6-diene-3,20-diol (XXXIV). XXXIV in C6H6 refluxed with 50 g. MnO2 gave 3.27 g. retropregna-4,6-dien-20-ol-3-one, m. 198-8.5° (Me2CO), and a second C-20 isomer, m. 173-5°. Retropregna-4-en-20-ol-3-one (XXXV) treated with NaH and HCO2Et and the Na product acidified with 5% HCl gave 2-hydroxymethyleneretropregn-4-en-20-ol-3-one, m. 94-9° (Et2O), [α]21D -155° (alc.). VII (2 g.) in 40 ml. tetrahydrofuran reduced with LiAlH4 gave retropregn-4-ene-3,20-diol and this product refluxed with MnO2 in C6H6 gave 1.69 g. XXXV, m. 174-6° (Me2CO-hexane). XIV (1 g.) in 10 ml. CH2Cl2 treated with alc.-HCl gave 3-ethoxyretropregna-3,5,7-trien-20-one, m. 115-16° (MeOH). XXXII (7.5 g.) in 200 ml. AcOH refluxed 4.5 hrs. with 21 g. KOAc gave 2-acetoxyretroprogesterone, m. 195.5-7.0°(alc.). XXXIII

treated with monoperphthalic acid in EtOAc gave 6-hydroxyretroprogesterone (XXXVI). Acetylation of XXXVI gave 6-acetoxyretroprogesterone, m. 177-8.5° (alc.). XX was converted into the 17-caproate, m. 110-12.5° (E2O-hexane). 3,17-Diacetoxyretropregna-3,5-dien-20-one (13.2 g.) in 950 ml. dioxane and 40 ml. H2O treated 1 hr. at room temperature with passage of perchloryl fluoride gave 6α-fluoro-17α-acetoxyretroprogesterone, m. 177-9° (Me2CO-hexane), and 6β-fluoro-17α-acetoxyretroprogesterone, m. 197.5-8.5° (Me2CO), plus 3,6,20-trioxoretropregnan-17α-ol 17-acetate, m. 241-4° (Et2O-C6H6-Me2CO). XIV (25 g.) treated with BzO2H gave 6,7-oxidoretroprogesterone (XXXVII), m. 187-90° (EtOAc), and some 6-chloro-7-hydroxyretroprogesterone (XXXVIII) due to splitting of the **epoxy** bond of XXXVII during chromatography. XXXVIII treated with HCl 3 hrs. at room temperature gave 6-chloro-6-dehydroretroprogesterone. XXVIII (4 g.) and 4 g. dichlorodicyanobenzoquinone in C6H6 refluxed 7.5 hrs. over 0.4 g. p-nitrophenol gave 2 g. 1-dehydro-6β-fluororetroprogesterone, m. 208-11° (EtOAc). 17α-Acetoxyretroprogesterone in MeOH treated 6 days with CuBr gave 6-dehydro-6-methoxy-17α-acetoxyretroprogesterone, m. 275-80° (alc.). XIV (3 g.) in 3 ml. thioacetic acid refluxed 2.5 hrs. gave 7-acetylthioretroprogesterone, m. 133-5° (Me2CO-hexane). VII similarly treated with CuBr gave 6-dehydro-6-methoxyretroprogesterone, m. 206-8°. XI (3 g.) in 30 ml. MeOH refluxed 10 min. with 1.6 ml. **pyrrolidine** gave 3.31 g. 3-(N-**pyrrolidino**)retroandrosta-3,5-dien-17-one (XXXIX). XXXIX (3.3 g.) refluxed 5 hrs. with a solution containing methallyl-magnesium chloride and worked up gave 2.52 g. 17α-(2-methallyl)retrotestosterone, m. 91-3° (MeOH). Dried sample from Et2O m. 106-8°. I (60 g.) and 6 g. CuCl in 500 ml. tetrahydrofuran stirred 3 hrs. with solution prepared from 100 ml. MeBr, 25 mg. Mg, and 5 g. CuCl in 200 ml. tetrahydrofuran gave 29 g. 7-methyllumista-4,22-dien-3-one (XL), m. 94.5-5.5° (ligroine), [α]22D -150.5°. XL upon ozonization gave 3-oxo-7-methylretrobisnorchol-4-en-22-al (XLI), m. 161.5-2.0°, [α]23D -148. XLI (4.65 g.) in 100 ml. C6H6 refluxed 5 hrs. with 2 ml. piperidine and 2 mg. p-MeC6H4SO3H gave 7-methyl-22-(N-piperidyl)-retrobisnorchola-4,20(22)-dien-3-one (XLII), m. 153.5-4.5°, [α]23D -120°. XLII (1.96 g.) treated with Na2CR2O7 in AcOH gave 7-methylretroprogesterone, m. 206-8°, [α]25D -57°. XXXIX treated with CH2:CHCH2MgCl gave 17α-allylretrotestosterone, m. 74-8°. XX (1 g.) heated 45 min. at 80° with 3.3 g. trimethylacetic acid and 1 ml. trifluoroacetic anhydride gave 6-dehydro-17α-hydroxyretroprogesterone 17-pimalate, m. 214-16°. 17α-Acetoxyretroprogesterone (4 g.) refluxed 15 hrs. with 2.7 g. dichlorodicyanobenzoquinone in 200 ml. C6H6 gave 1-dehydro-17α-acetoxyretroprogesterone, m. 183-4.5°. XIa treated with Ac2O-p-MeC6H4SO3H and then with concentrated HCl in MeOH gave 17α-ethynylretrotestosterone 17-acetate, m. 183-4° (Me2CO). VII by hydroxylation (microbiol.) gave 16α-hydroxyretroprogesterone (XLIII), m. 172.5-4.5°, [α]25D -92.3°. Dehydration of XLIII gave 16-dehydro retroprogesterone, m. 165-7°. Microbiol. hydroxylation of VII gave 15α-hydroxyretroprogesterone, m. 203-5°, [α]D -23°. Oxidation of 11,17α,21-trihydroxyretroprogesterone 21-acetate with CrO3 gave retrocortisone 21-acetate, m. 275° (decomposition). Microbiol. hydroxylation of XIV gave 6-dehydro-16α-hydroxyretroprogesterone (XLIV), m. 200-3°, [α]D -526°. Dehydration of XLIV gave 6,16-bisdehydroretroprogesterone, m. 163-5°. Hydroxylation of VII gave 11-hydroxyretroprogesterone (XLV). Oxidation of XLV with CrO3 gave 11-oxoretroprogesterone, m. 158-60°. Hydroxylation of XVIII gave 11,17α-dihydroxyretroprogesterone (XLVI), m. 202-6.5° (decomposition), [α]D -118°. XLVI oxidized as above gave 11-oxo-17α-hydroxyretroprogesterone, m. 240-5°. XXIII was converted into 2-fluoro-6-dehydro-17α-acetoxyretroprogesterone, m. 204-5°. Degradation of the side-chain of 2-

fluorodihydroisolumisterone gave 2-fluororetroprogesterone, m. 162-4°. II was converted to 2-(ethoxyoxalyl)lumista-4,22-dien-3-one then to 2-methyllumista-4,22-dien-3-one (XLVII). XLVII ozonized, treated with Ac2O, and oxidized gave 2-methylretroprogesterone, m. 126-7°. Degradation of the side chain of 2-methyllumista-4,6,22-trien-3-one gave 2-methyl-6-dehydroretroprogesterone, m. 168.5-70.0°. Retroandrost-4-en-17-one (XLVIII) treated with CH2:CHCH2MgCl gave 17α-allylretroandrost-4-en-17-ol, m. 79-86°. XLVIII with KC.tplbond.CH in iso-PrOH gave 17α-ethynylretroandrost-4-en-17-ol, m. 74-5°. Treatment of the Na enolate of the 21-ethoxy oxalate of XXVI with perchloryl fluoride in MeOH and NaOMe gave after refluxing with KOAc 21-fluoro-1,6-bisdehydroretroprogesterone, m. 154-5°. XI (1.13 g.) reduced with 550 mg. LiAlH4 gave retroandrost-4-en-3,17β-diol (XLIX), m. 117-18° (ligroine). Crude XLIX shaken 17 hrs. in 60 ml. CHCl3 with 6 g. MnO2 gave retrotestosterone (L), m. 115-6° (E+2O), [α]23D -154°. L gave the β-phenylpropionate, m. 73-4° (MeOH). L (5 g.) treated as above with chloranil 1.43 g. 6-dehydroretrotestosterone (LI), m. 174-5° (E2O). LI (360 mg.) afforded 233 mg. propionate, m. 115-17° (MeOH). L (0.5 g.) treated with 0.5 g. Li in 75 ml. NH3 and 50 ml. E2O and the product esterified gave 270 mg. bis(3,5-dinitrobenzoate) of retro-5-androstane-3,17β-diol, m. 237-42°(CH2Cl2-Me2CO). L (1 g.) in 35 ml. C6H6 refluxed 48 hrs. with 1 g. SeO2 and 0.6 ml. H2O and the product chromatographed on Al2O3 gave 98 mg. 1-dehydroretrotestosterone, m. 175-7° (hexane-CH2Cl2). L (1.14 g.) was converted into enol of 2-(ethoxyoxalyl)retrotestosterone (LII). LII (1.3 g.) refluxed 18 hrs. with 2 ml. MeI in 25 ml. Me2CO and 1 g. K2CO3 and chromatographed on Al2O3 gave 207 mg. 2-methylretrotestosterone, m. 177-9.5° (Et2O-hexane). Retroandrosta-4,6-dien3,17-**dione** (LIIa) treated with LiAlH4 gave retroandrosta-4,6-diene-3,17β-diol (LIII), m. 140-4 (decomposition). Crude LIII refluxed 30 hrs. with MnO2 in C6H6 gave 3 g. LI. 6-Bromoretrotestosterone 17-acetate treated with C5H5N gave 17-acetate of LI, m. 131-3° L (1 g.) and 0.005 ml. concentrated H2SO4 refluxed 3 hrs. with 5 ml. isopropenyl acetate gave 0.9 g. 3,17β-diacetoxyretroandrosta-3,5-diene, m. 118-19 (MeOH). L (1g.)added to 0.4 g. K in 20 ml. tert-BuOH, left 3.5 hrs. at room temperature with 1.3 ml. MeI gave 4,4-dimethylretroandrost-5-en-17β-ol-3-one, m. 152.5-3.5°. L gave thep-hexyloxyphenylpropionate and propionate (LIV), m. 107-8°.

LIV acetylated with isopropenyl acetate in the presence of traces of concentrated H2SO4 gave 3-acetoxyretroandrosta-3,5-dien-17β-ol 17-propionate, m. 102-4°. 6-Bromoretrotestosterone 17-acetate (410 mg.) and 1.3 g. KOAc in 10 ml. AcOH refluxed 4 hrs. gave 2-hydroxyretrotestosterone 2,17-diacetate, m. 184-6°. 3,17-Diacetoxyretroandrosta-3,5-diene treated with KOAc in AcOH, then with Br in AcOH, and worked up gave 6-bromoretrotestosterone 17-acetate, m. 130° (decomposition). 3,17°-Diacetoxyretroandrosta-3,5-diene (4 g.) in 178 ml. EtOAc containing 14.3 mg. monoperphthalic acid/ml. left overnight at 5° gave mixture (LV) of 6α- and 6β-hydroxyretrotestosterone 17-acetate, m. 167-70°. LV (2.6 g.) in 10 ml. C5H5N and 10 ml. Ac2O left 20 hrs. at room temperature and the product separated gave one isomer of 6,17-diacetoxyretrotestosterone, m. 178-80°, and the other isomer, m. 116-17°. LI was converted to the 17-palmitate, m. 58.5-9.0°. L treated with NaH and HCO2Et and then with 5% HCl gave 2-hydroxymethyleneretrotestosterone (LVI), m. 98-120° (aqueous alc.). LVI (5 g.) in 13 ml. alc. refluxed 3 hrs. with 2.5 ml. N2H4.H2O in 40 ml. alc. gave 3.5 g. 17β-hydroxyretroandrost-4-eno[3,2-c]pyrazole, m. 259-63°, [α]24D -149° (alc.). LI (2 g. (in 10 ml. pyridine left 18 hrs. at room temperature with 2.5 g. p-hexyloxyphenylpropionyl chloride gave 3.9 g. resinous 6-dehydroretrotestosterone 17-(p-hexyloxyphenylpropionate). LI treated 16 hrs. at 60**.degree** . with succinic anhydride gave the 17-hemisuccinate, **m.** 178-93.5-201.5-203.5°. LI also gave the 17-phenylpropionate, m. 93-4° (MeOH). LIIa treated with Br in CCl4 gave

4-bromoretroandrosta-4,6-dien-3,17-dione, m. 130-50°. L 17-propionate (1.2 g.) in 150 ml. C6H6 treated with 9 ml. (CH2OH)2 gave 3,3-ethylenedioxyretroandrosta-3,5-dien-17β-ol-17-propionate, m. 66-8β. XXXIX (3 g.) treated with MeMgBr gave 17α-methylretrotestosterone (LVII), m. 133-4°. LIIa similarly gave 3-ethoxyretroandrosta-3,5,7-trien-17-one, m. 118-19.5°. LIIa (1 g.) in 15 ml. CH2Cl2 left 0.5 hr. at 0° with dry HCl in MeOH gave 404 mg. 3-methoxyretroandrosta-3,5,7-trien-17-one, m. 139-40°. L (2.5 g.) converted to the 17-hexahydrobenzoate, m. 71-3° (petr. ether). LVII (2 g.) and dichlorodicyanobenzoquinone in C6H6 refluxed 7 hrs. gave 1-dehydro-17α-methylretrotestosterone, m. 163-4°. XI treated with isopropenyl acetate gave 3-acetoxyretroandrosta-3,5-dien-17-one, m. 142-3°. L (1.564 g.) in 6.25 ml. C5H5N treated 24 hrs. at room temperature with 1.56 g. p-toluenesulfonyl chloride gave the 17-tosylate, m. 164.5-5.5°. The tosylate treated with KOAc in HCONMe2 and the resin hydrolyzed with KOH solution gave retroandrosta-4,16-dien-3-one and L. L was converted into the 17-acetate, m. 128.5-30.0°. 3,17β-Diacetoxyretroandrosta-3,5-diene (10.3 g.) treated in dioxane with perchloryl fluoride and chromatographed on silica gel gave 6α-fluororetrotestosterone 17-acetate, m. 129.5-30.5°. Microbiol. hydroxylation of L gave 16α-hydroxyretrotestosterone, m. 210-12°, [αID -167°. XXIII converted into 2-fluororetrobisnorchol-3-one-4-en-22-al, then into 2-fluororetrobisnorchol-3-one-4,17(20)-dien-22-al, 2-fluororetroandrost-4-en-3,17-dione, 2-fluororetroandrost-4-en-3,17-diol, 2-fluororetrotestosterone, and finally 2-fluoro-6-dehydroretrotestosterone, m. 90-5° and 142-3.5°. XI reduced with NaBH4 in alc.-H2O gave 3,17β-dihydroxyretro-5-androst-4-ene and 8,17β-dihydroxyretroandrostane (LVIII), m. 156-8°. LVIII oxidized with CrO3 in Me2CO containing H2SO4 gave retro-5-androstane-3,17-dione, m. 114-15.5°. 17α-Methylretroandrost-4-en-17-ol was obtained by treatment of retroandrost-4-en-17-one (LIX) with MeMgI. L (2 g.) in 3 ml. Et2O and 6.5 ml. AcOH stirred 1 hr. with 0.72, ml. 1,2-ethanedithiol and 0.85 ml. BF3.Et2O gave 3-ethylene dithioketal of L, m. 166-7.5°. This ketal (0.5 g.) in 2.5 ml. tetrahydrofuran added to 15 ml. liquid NH3 and 5 ml. tetrahydrofuran, stirred 15 min. with 0.4 g. L gave 3-deoxyretrotestosterone (LX). LX oxidized with CrO3 in Me2CO gave LIX, m. 89-90.5°. L with AcCl gave the 17-acetate, m. 113-14.50. XLII (1 g.) in 50 ml. CH2Cl2 treated in 20 min. at -55° with 0.15 ml. Br in 6 ml. CH2Cl2, mixture heated to 0°, and product heated with C5H5N for 1 hr. at 70° gave 7-methylretrobisnorchola-4,17(20)-dien-3-on-22-al (LXI), m. 182-3.5°. LXI suspended in MeOH treated with NaCN, AcOH, and MeOH 2 hrs. from -20° to +5° and kept 40 hrs. at 5° gave 7-methylretroandrost-4-ene-3,17-dione (LXII), m. 196-7°. LXII was reduced to give 7-methylretroandrost-4-ene-3,17β-diol (LXIII), m. 80-95°. LXIII oxidized as above gave 7-methylretrotestosterone, m. 146.5-50.0°. 3,17β-Diacetoxyretroandrosta-3,5-diene (3 g.) in 60 ml. Et2O treated with 6.4 g. KOAc in 120 ml. 85% AcOH, and treated 5-10 min. at 0° with 0.57 g. Cl gave 6-chlororetrotestosterone 17-acetate, m. 176-8°. II treated with Et orthoformate in C6H6 and alc. gave 3-ethoxylumista-3,5,22-triene (LXIV), m. 76-7.5° (alc.). LXIV (12.7 g.) in 60 ml. dioxane and 4.8 ml. C5H5N left 45 hrs. at room temperature with 20 g. CBr4 gave 7.46 g. 6-tribromomethyldihydroisolumisterone (LXV), m. 132-3.5° (Me2CO-MeOH). LXV (100 mg.) in 15 ml. alc. heated with 15 ml. of a strong anion exchange resin gave 6-dibromomethylenedihydroisolumisterone, m. 100-2.5°, [α]23D 10°. XI was converted into 3-(1-pyrrolidino)retroandrosta-3,5-dien-17-one (LXVI). LXVI treated with CH2:CMeCH2MgCl gave 17α-(2-methallyl)retrotestosterone, m. 106-8°. Similarly LXVI gave 17α-allylretrostesterone, m. 76-8°. Retroandrosta-4,6-diene-3,17-dione was converted into 3,7-di(1-pyrrolidino)retroandrosta-3,5-dien-17-one, and then alkylated to give 6-dehydro-17α-(2-methallyl)retrotestosterone. Many related compds. were prepared by the above described procedures.

L10 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI Steroid alkaloids. XXVIII. New method of preparation of 18-substituted pregnane derivatives from conessine
GI For diagram(s), see printed CA Issue.
AB 20(N)-Conanene derivs. treated with 1 mole-equivalent peracid gave the corresponding **oxiranes**, which were converted into 18-substituted pregnane derivs. N-Demethyl-5α-conan-20(N)-ene (1 g.) in 20 cc. CHCl3 treated with stirring with 0.593 g. p-O2NC6H4CO2OH (I) in portions at 15-min. intervals and stirred 15 min. yielded 0.99 g. N-demethyl-20,N-oxido-5α-conan-3-one (II), m. 140-1° (95% EtOH) (sublimed at 135°/0.01 mm.), [α]20D 53° (c 1.24) (all rotations in CHCl3). II (1.67 g.) in 10 cc. MeOH and a few crystals p-MeC6H4SO3H refrigerated 3 hrs. yielded 1.46 g. 3,3-dimethoxy-20,N-oxido-N-demethyl-5α-conanine (III), m. 209-10° (Me2CO), [α]20D 31° (c 1). III (1.02 g.) in 20 cc. CH2Cl2 and 1 g. Na2CO3 treated with stirring with 0.77 g. I gave 0.856 g. 3,3-dimethoxy-18-oximo-5α-pregnan-20-one (IV), decompose .apprx.130° with a change at 85-90° (MeOH or Me2CO), [α]20D 7° (c 1). IV (0.254 g.) in 10 cc. CH2Cl2 treated 5 min. with 10 cc. N HCl gave 0.149 g. 18-oximino-5α-pregnane-3,20-**dione** (V), m. 186-7° (Me2CO). 13β-Cyano-18-nor-5α-pregnane-3,20- **dione** (VI) (1.8 g.) in 30 cc. MeOH stirred with a few crystals p-MeC6H4SO3H yielded 1.32 g. 3,3-dimethoxy-13β-cyano-18-nor-5α-pregnan-20-one (VII), m. 190-1° (MeOH and sublimed in vacuo), [α]20D 17° (c 1.1). VII (0.258 g.) in 20 cc. CH2Cl2 treated 1 hr. with 20 cc. N HCl yielded 0.229 g. VI, m. 192-3° (95% EtOH), [α]20D 41° (c 1.06). N-Demethyl-5α-conan-20(N)-ene (4 g.) in 25 cc. CHCl3 added during 10 min. with stirring to 6 g. I in 130 cc. CHCl3 and stirred 50 min. gave 2.767 g. V, m. 185-6° (Me2CO), containing a small amount of a by-product. V (0.703 g.) in 10 cc. dry C5H5N treated with 0.3 cc. POCl3 gave 0.546 g. VI, m. 182-3°. II (0.5 g.) in 10 cc. CHCl3 and 0.5 g. Na2CO3 treated during 15 min. with 0.426 g. I gave 0.328 g. mixture, m. 199-200° (Me2CO); a 0.966-g. portion treated with 13 cc. dry C5H5N and 0.86 cc. POCl3 gave 0.22 g. VI. VI (1 g.) in 17 cc. tetrahydrofuran added dropwise with stirring at 0° to (tert-BuO)3AlLiH from 0.25 g. LiAlH4 in 10 cc. tetrahydrofuran, stirred 8 min. at 0° and 1 hr. at room temperature, and poured into 100 cc. 40% aqueous KOH gave 0.918 g. lacquer, which dissolved in 170 cc. absolute EtOH and refluxed 15 hrs. with 160 cc. 2N HCl yielded 0.761 g. crude product; the product chromatographed on 22 g. Al2O3 yielded 0.071 g. 5α-pregnan-20β-ol-3-on-18-oic acid 18,20-lactone, m. 246-8° (Me2CO), [α]20D 28° (c 1),and 0.06 g. 5α-pregnan-20α-ol-3-on-18-oic acid 18,20-lactone, m. 176-7° (Me2CO), [α]20D 17° (c 1).

L10 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
TI **Epoxides** by the action of diaryldiazomethanes on ketones
AB A series of aromatic and heterocyclic ketones was converted with Ph2CN2 (I) to **epoxides** without the occurrence of ring enlargements and chain extensions observed in the reactions with CH2N2. The different mechanism in the addition of I to the CO group and to alkene derivs. is discussed. Isatin (II) (4.9 g.) and 7.0 g. I in 100 cc. C6H6 refluxed 3.5 hrs. yielded 8.4 g. 3,3'-oxido-3-diphenyhnethyloxindole (III) (R = H) (IIIa), m. 238° (PhMe), yellow in concentrated H2SO4. 3-Diphenylmethyleneoxindole (IV) (0.20 g.) in 5 cc. C6H6 and 25 cc. EtOH treated with 5 cc. 4N NaOH and 10 cc. H2O2 12 hrs. at room temperature yielded 0.15 g. IIIa, m. 238° (MePh). Oxindole (1.3 g.) and 3.0 g. BzPh in 20 cc. Me3COH refluxed 7 hrs. with 0.5 g. Na in 50 cc. tert-BuOH gave 2.1 g. IV, yellow crystals, m. 240° (EtOH and then ligroine, b. 100-40°). IIIa (0.8 g.) in 30 cc. AcOH with 1 g. KI refluxed 5 hrs. yielded BzPh, oxindole, m. 120°, and IV, m. 240°. IIIa (0.6 g.) in 25 cc. AcOH refluxed 0.5 hr. with 5 cc. concentrated HCl gave 0.3 g.

BzPh and 0.1 g. isoindigo (IVa, R = H) (sublimed in vacuo at 300°). 1-Methylisatin (11.5 g.) and 15 g. I in 150 cc. MePh refluxed 2 hrs. gave 12 g. III (R = Me) (V), m. 176° (EtOH). V (0.5 g.) in 25 cc. AcOH and 10 cc. concentrated HCl refluxed 0.5 hr. gave 0.2 g. BzPh and IVa (R = Me), red needles, m. 265° (EtOH). IIIa (1.5 g.) and 1.5 g I in 50 cc. C6H6 refluxed 24 hrs. and evaporated, and the residue kept 24 hrs. in Et2O at -20° yielded 1.8 g. III (R = CHPh2) (VI), m.155°. II (1.5g.) and 5.0 cc. I in 75 cc. C6H6 refluxed 24 hrs. gave similarly 2.9 g. VI, m. 155° (EtOH). VI (0.30 g.) in a little AcOH refluxed 0.5 hr. with 0.50 g. Na2Cr2O7 gave 0.15 g. N-diphenylmethylisatin, m. 168°. VI (0.47 g.) in 50 cc. EtOH and 30 cc. concentrated HCl refluxed 3 hrs. yielded 50 mg. IVa (R = CHPh2), red crystals, m. 275° (EtOH). Trioxohydrindene (0.9 g.) and 1.25 g. I in 20 cc. C6H6 heated 10 min. after the violent gas evolution had subsided gave 1.7 g. 2,2'-oxido-2-diphenylmethyl-1,3-dioxohydrindene (VII), m. 155°. VII (0.30 g.) in 10 cc. EtOH refluxed with 1 drop concentrated HCl gave 50 mg. hydrindantin. 9-Dibenzoylmethylenexanthene (5.0 g.) in 50 cc. C6H6 and 100 cc. MeOH treated with stirring at room temperature with 5 cc. 4N NaOH and 10 cc. 30% H2O2 and diluted after 1.5 hrs. with 200 cc. H2O yielded 4.9 g. 9,9'-oxido-9-dibenzoylmethylxanthene (VIII), yellow crystals, m. 178° (EtOH). Ph(CO)3Ph (2.70 g.) in 20 cc. dry C6H6 treated with 2.50 g. diazoxanthene (IX) in 200 cc. petr. ether overnight gave 1.88 g. VIII, m. 178° (MeOH). VIII (0.30 g.) in 20 cc. EtOH and 10 cc. C6H6 refluxed 1 hr. with 1 cc. concentrated HCl yielded 0.13 g. xanthone, m. 174° (EtOH). 1,8-Diazafluorenone (0.60 g.) and 0.70 g. I in 25 cc. C6H6 refluxed 5 hrs. and evaporated, and the residue kept in Me2CO 24 hrs. at -20° gave 0.85 g. 9.9'-oxido-9-diphenylmethyl-1,8-diazafluorene (X), m. 211-12° (Me2CO). 9-Diphenylmethylene-1,8-diazafluorene (0.22 g.) in 10 cc. C6H6 and 40 cc. EtOH treated with stirring at room temperature with 10 cc. 4N NaOH and 15 cc. 30% H2O2 overnight, yielded 0.07 g. X, m. 211-12° (Me2CO). X (0.20 g.) in 20 cc. 1:4 concentrated HCl-H2O refluxed 15 min. yielded 95 mg. BzPh; the aqueous phase yielded 70 mg. 1,8-diazafluorenone, m. 210°. I (7.0 g.) in 50 cc. C6H6 added slowly dropwise with stirring to 5.0 g. acenaphthenequinone (XI) in 200 cc. refluxing C6H6, refluxed 2 hrs., filtered from 2.7 g. XI, m. 260°, and cooled gave an addnl. 2.2 g. XI; the mother liquor yielded 3.5 g. benzophenone azine (XII), m. 164°. XI (1.00 g.) in 75 cc. MeOH and 75 cc. hot C6H6 refluxed 1 hr. with 1.20 g. IX in 100 cc. petr. ether yielded 0.90 g. unreacted XI. α,α'-Dipyridyl ketone (0.6 g.) and 0.7 g. I in 25 cc. C6H6 refluxed 3 hrs. yielded XII, m. 164°. Fluorenone did not react with I in refluxing C6H6-MeOH.

=> d L10 2,16 all

L10 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:43845 CAPLUS
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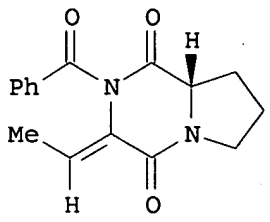
TI Stereoselective **epoxidation** and bromoalkoxylation with 3-ylidenepyrazine-2,5-**diones**
AU Bartels, Annett; Jones, Peter G.; Liebscher, Jurgen
CS Institut fur Chemie, Humboldt-Universitat Berlin, Berlin, 12489, Germany
SO Synthesis (2003), (1), 67-72
CODEN: SYNTBF; ISSN: 0039-7881
PB Georg Thieme Verlag
DT Journal
LA English
CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 75
OS CASREACT 138:353941
GI



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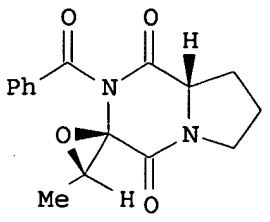

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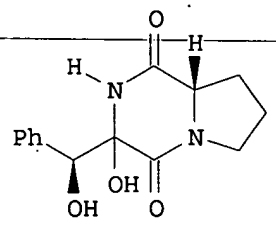
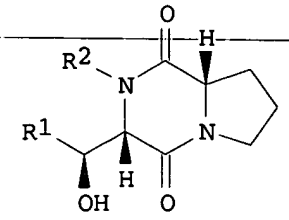


III



IV

AB 3-Ylidenepyrazine-2,5-**diones**, e.g., I, were stereoselectively **epoxidized** by dimethyldioxirane giving access to spirooxiranes, e.g., II, and diols, e.g., III. Bromohydroxylation and bromoalkoxylation of 3-ylidenepyrazine-2,5-**diones** produced high yields of optically active 3-(1-bromoalkyl)pyrazine-2,5-**diones** with a 3-hydroxy or 3-alkoxy function, resp. Whereas direct hydrogenation of **epoxides** afforded epimeric mixts. of 3-(1-hydroxyalkyl)pyrazine-2,5-**diones**, the highly stereoselective transformation into IV (R1 = Me, i-Pr, R2 = PhCO; R1 = Ph, R2 = H)was possible by primary acid cleavage of the **oxirane** ring followed by hydrogenation of the resulting keto-enol mixts.

ST piperazinedione **epoxidn**; spirooxirane prepn; ylidenepiperazinedione bromoalkoxylation; bromoalkylpiperazinedione prepn

IT Crystal structure
Molecular structure
(of (bromobenzyl)methylmethoxypyrrolidinopiperazinedione)

IT Asymmetric synthesis and induction
(stereoselective preparation of (hydroxyalkyl)hydroxypyrrolidinopiperazinedi ones via **epoxidn.** of chiral alkylidenepyrrolidinopiperazinedi ones with dimethyldioxirane)

IT **Epoxidation**
(stereoselective; stereoselective preparation of (hydroxyalkyl)hydroxypyrrolidinopiperazinediones via **epoxidn.** of chiral alkylidenepyrrolidinopiperazinediones with dimethyldioxirane)

IT 518345-86-3P
RL: BYP (Byproduct); PREP (Preparation)
(byproduct in the preparation of (hydroxyalkyl) **pyrrolidinopiperazinediones**)

IT 518345-66-9P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation and crystal structure of (bromoalkyl)alkoxypyrrolidinopiperazinediones via bromoalkoxylation of chiral alkylidenepyrrolidinopiperazinediones with alcs.)

IT 67-63-0, Isopropanol, reactions 114673-62-0 214849-88-4 286838-82-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective preparation of (bromoalkyl)alkoxypyrrolidinopiperazinedione s via bromoalkoxylation of chiral alkylidenepyrrolidinopiperazinediones with alcs.)

IT 518345-56-7P 518345-58-9P 518345-60-3P 518345-62-5P 518345-64-7P 518345-68-1P 518345-70-5P
RL: SPN (Synthetic preparation); PREP (Preparation)

(stereoselective preparation of (bromoalkyl)alkoxypyrrolidinopiperazinedione
s via bromoalkoxylation of chiral alkylidenepyrrolidinopiperazinediones
with alcs.)
IT 518345-50-1P 518345-52-3P 518345-54-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of (hydroxyalkyl)hydroxypyrrolidinopiperazinedi
ones via **epoxidn.** of chiral alkylidenepyrrolidinopiperazinedi
ones with dimethyldioxirane)
IT 518345-74-9P 518345-76-1P 518345-78-3P 518345-79-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(stereoselective preparation of (hydroxyalkyl)
pyrrolidinopiperazinediones via catalytic hydrogenation of
spiroepoxy- or acylpyrrolidinopiperazinediones)
IT 518345-72-7P 518345-82-9P 518345-84-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of (hydroxyalkyl)
pyrrolidinopiperazinediones via catalytic hydrogenation of
spiroepoxy- or acylpyrrolidinopiperazinediones)
IT 144-98-9P, allo-Threonine
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of allo-threonine via acid hydrolysis of chiral
(hydroxyethyl)**pyrrolidinopiperazinedione**)
IT 126253-50-7 167938-42-3 518345-36-3 518345-40-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereoselective preparation of spiroepoxypyrrolidinopiperazinediones via
epoxidn. of chiral alkylidenepyrrolidinopiperazinediones with
dimethyldioxirane)
IT 167864-24-6P 167864-25-7P 518345-45-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(stereoselective preparation of spiroepoxypyrrolidinopiperazinediones via
epoxidn. of chiral alkylidenepyrrolidinopiperazinediones with
dimethyldioxirane)
IT 518345-48-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(stereoselective preparation of spiroepoxypyrrolidinopiperazinediones via
epoxidn. of chiral alkylidenepyrrolidinopiperazinediones with
dimethyldioxirane)
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Adam, W; Chem Ber 1991, V124, P277
(2) Anon; deposit@ccdc.cam.ac.uk
(3) Bartels, A; Tetrahedron Lett 1995, V36, P3673 CAPLUS
(4) Gelin, J; J Org Chem 1993, V58, P3473 CAPLUS
(5) Hoare, J; J Chem Soc, Chem Commun 1981, P1126 CAPLUS
(6) Itoh, K; Heterocycles 1997, V45, P1345 CAPLUS
(7) Liebscher, J; Chem Soc Rev 1999, V28, P251 CAPLUS
(8) Marcuccio, S; Aust J Chem 1985, V38, P1785 CAPLUS
(9) Marcuccio, S; Aust J Chem 1985, V38, P343 CAPLUS
(10) Marshall, J; Synth Commun 1975, V5, P237 CAPLUS
(11) Messeguer, A; Tetrahedron 1991, V47, P1291 CAPLUS
(12) Moyroud, J; Tetrahedron 1996, V52, P8525 CAPLUS
(13) Nemes, C; J Org Chem 1994, V59, P900 CAPLUS
(14) Oh, Y; J Org Chem 1992, V57, P3662 CAPLUS
(15) Poisel, H; Chem Ber 1973, V106, P3408 CAPLUS
(16) Shin, C; Bull Chem Soc Jpn 1983, V56, P2652 CAPLUS
(17) Yates, P; Can J Chem 1983, V61, P1397 CAPLUS

L10 ANSWER 16 OF 19 CAPLUS
AN 1974:570470 CAPLUS
DN 81:170470
ED Entered STN: 12 May 1984
TI Heat-hardenable compositions
IN Lefebvre, Gerard; Rollet, Bernard

PA Rhone-Poulenc S. A.
SO Ger. Offen., 19 pp.
CODEN: GWXXBX
DT Patent
LA German
IC C08G
CC 36-3 (Plastics Manufacture and Processing)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2354654	A1	19740516	DE 1973-2354654	19731031
	DE 2354654	B2	19771020		
	FR 2204655	A1	19740524	FR 1972-38609	19721031
	NL 7314558	A	19740502	NL 1973-14558	19731023
	DD 107300	C	19740720	DD 1973-174312	19731026
	ZA 7308286	A	19740925	ZA 1973-8286	19731026
	US 3875113	A	19750401	US 1973-409935	19731026
	JP 50046799	A2	19750425	JP 1973-120615	19731026
	JP 51035520	B4	19761002		
	BR 7308444	A0	19740905	BR 1973-8444	19731029
	AU 7361925	A1	19750501	AU 1973-61925	19731029
	BE 806759	A1	19740430	BE 1973-137276	19731030
	GB 1412224	A	19751029	GB 1973-50434	19731030
	CH 587883	A	19770513	CH 1973-15252	19731030
	CA 1014697	A1	19770726	CA 1973-184592	19731030
	IT 999151	A	19760220	IT 1973-30828	19731031
PRAI	FR 1972-38609		19721031		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
DE 2354654	IC	C08G

AB Reaction of **epoxy** resins with bis(4-aminophenyl)methane [101-77-9] and 4-maleimido-4'-acetamidodiphenylmethane [53184-84-2], 4,4'-diphenylmethanebismaleimide [13676-54-5] or 4-maleimido-4'-acetoxysuccinimidodiphenylmethane [53184-85-3] gave heat hardenable moldings.

ST **epoxy** resin heat hardenable; maleimido deriv modified **epoxy**; diaminodiphenylmethane modified **epoxy**

IT **Epoxy** resins
RL: USES (Uses)
(reaction products with bis(aminophenyl)methane and mono- and (or) diimides, heat-hardenable)

IT Phenol, polymer with formaldehyde, **oxiranylmethyl** ether, reaction products with bis(aminophenyl)methane and mono- and (or) diimides
RL: USES (Uses)
(heat-hardenable)

IT 101-77-9D, Benzenamine, 4,4'-methylenebis-, reaction products with **epoxy** resins and mono- and (or) diimides 13676-54-5D, 1H-**Pyrrole**-2,5-**dione**, 1,1'-(methylenedi-4,1-phenylene)bis-, reaction products with **epoxy** resins and bis(aminophenyl)methane 37307-44-1D, Epikote 173, reaction products with bis(aminophenyl)methane and mono- and diimides 53184-84-2D, Acetamide, N-[4-[[4-(2,5-dihydro-2,5-dioxo-1H-**pyrrol**-1-yl)phenyl]methyl]phenyl]-, reaction products with **epoxy** resins and bis(aminophenyl)methane 53184-85-3D, 1H-**Pyrrole**-2,5-**dione**, 1-[4-[[4-[3-(acetyloxy)-2,5-dioxo-1-**pyrrolidinyl**]phenyl]methyl]phenyl]-, reaction products with **epoxy** resins and bis(aminophenyl)methane 53228-95-8D, **Oxirane**, 2,2',2'',2'''-[1,2-ethanediylidenetetrakis(phenyleneoxymethylene)]tetrakis-, homopolymer, reaction products with bis(aminophenyl)methane, maleimidoacetamidodiphenylmethane, and diphenylmethanebismaleimide
RL: USES (Uses)
(heat-hardenable)

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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                  182.35     500.14

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                  -60.20     -60.20

STN INTERNATIONAL LOGOFF AT 11:46:25 ON 19 NOV 2004
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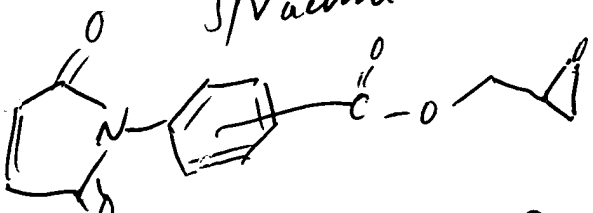
10/62,520

Connecting via Winsock to STN

11/19/04
Structure Search



Welcome to STN International! Enter x:x

LOGINID:SSSPTAAJP1626

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

See #9 of (3)

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 JUL 12 BEILSTEIN enhanced with new display and select options, resulting in a closer connection to BABS
NEWS 4 AUG 02 IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
NEWS 5 AUG 02 CAplus and CA patent records enhanced with European and Japan Patent Office Classifications
NEWS 6 AUG 02 The Analysis Edition of STN Express with Discover! (Version 7.01 for Windows) now available
NEWS 7 AUG 27 BIOCOMMERCE: Changes and enhancements to content coverage
NEWS 8 AUG 27 BIOTECHABS/BIOTECHDS: Two new display fields added for legal status data from INPADOC
NEWS 9 SEP 01 INPADOC: New family current-awareness alert (SDI) available
NEWS 10 SEP 01 New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!
NEWS 11 SEP 01 New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
NEWS 12 SEP 27 STANDARDS will no longer be available on STN
NEWS 13 SEP 27 SWETSCAN will no longer be available on STN
NEWS 14 OCT 28 KOREAPAT now available on STN
NEWS 15 NOV 18 Current-awareness alerts, saved answer sets, and current search transcripts to be affected by CERAB, COMPUAB, ELCOM, and SOLIDSTATE reloads

NEWS EXPRESS OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
NEWS HOURS STN Operating Hours Plus Help Desk Availability
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NEWS WWW CAS World Wide Web Site (general information)

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:11:18 ON 19 NOV 2004

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:11:29 ON 19 NOV 2004

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 17 NOV 2004 HIGHEST RN 783276-57-3
DICTIONARY FILE UPDATES: 17 NOV 2004 HIGHEST RN 783276-57-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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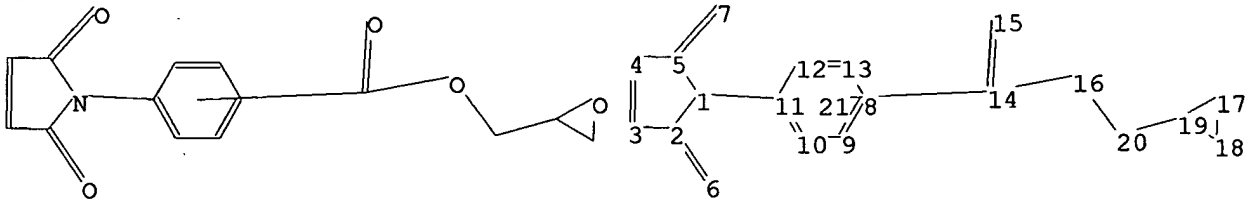

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ring nodes :
1 2 3 4 5 8 9 10 11 12 13 17 18 19
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ring bonds :
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exact/norm bonds :
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exact bonds :
19-20
normalized bonds :
8-9 8-13 9-10 10-11 11-12 12-13

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:CLASS 7:CLASS 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:Atom 18:Atom 19:Atom
20:CLASS 21:CLASS

L1 STRUCTURE UPLOADED

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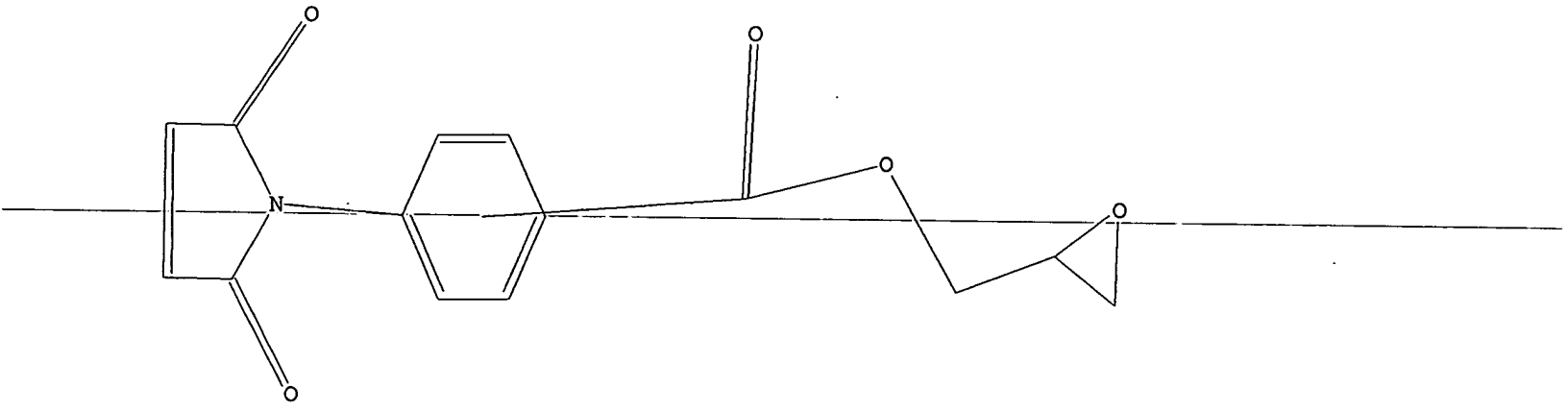
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 17 TO ITERATE

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FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 93 TO 587
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

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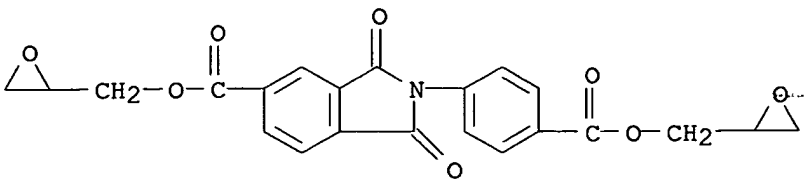
L3 15 SEA SSS FUL L1

=> d scan

L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[4-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester (9CI)
MF C22 H17 N O8
CI COM

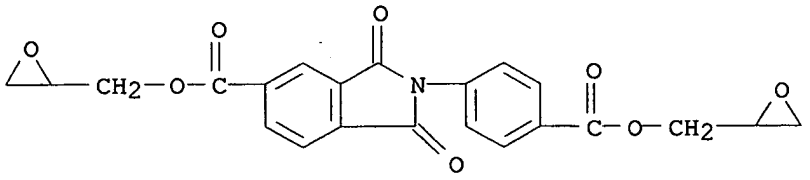


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

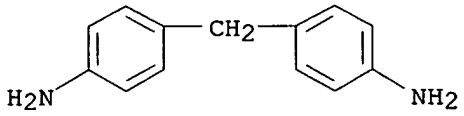
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):14

L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[4-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester, polymer with 4,4'-methylenebis[benzenamine] (9CI)
MF (C22 H17 N O8 . C13 H14 N2)x
CI PMS

CM 1

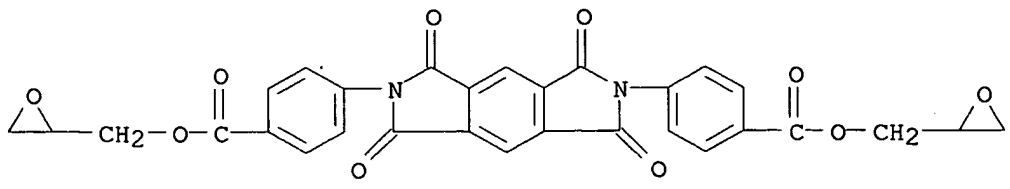


CM 2



L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1,4-Benzenedicarboxylic acid, polymer with bis(oxiranylmethyl) 4,4'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis[benzoate] and 1,2-ethanediol (9CI)
MF (C30 H20 N2 O10 . C8 H6 O4 . C2 H6 O2)x
CI PMS

CM 1



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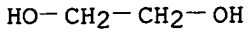

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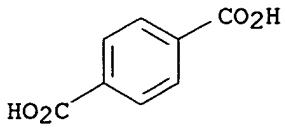
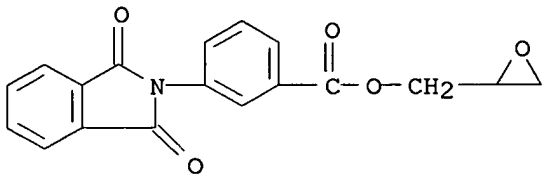


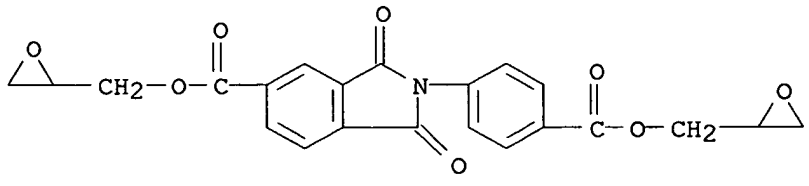
L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Benzoic acid, 3-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-, oxiranylmethyl ester (9CI)
MF C18 H13 N O5



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[4-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester, polymer with 1,3-benzenediamine (9CI)
MF (C22 H17 N O8 . C6 H8 N2)x
CI PMS

CM 1



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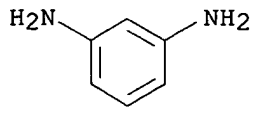
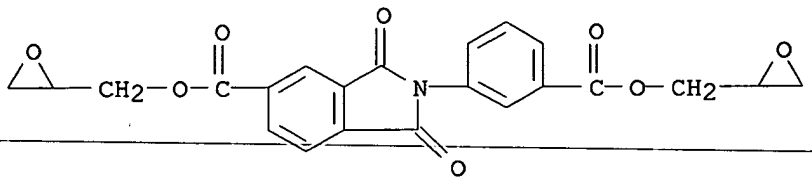


L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[3-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester, polymer with 4,4'-methylenebis[benzenamine] (9CI)
MF (C22 H17 N O8 . C13 H14 N2)x
CI PMS

CM 1



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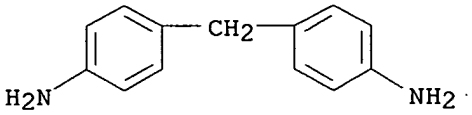
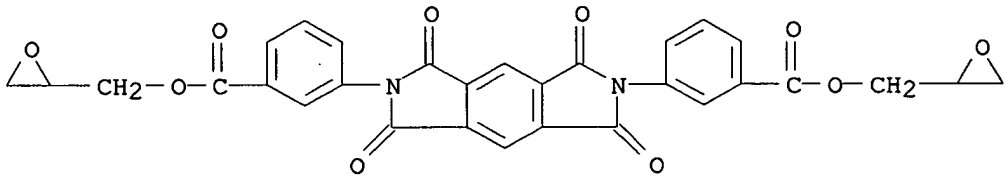


L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1,4-Benzenedicarboxylic acid, polymer with bis(oxiranylmethyl) 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis[benzoate] and 1,2-ethanediol (9CI)
MF (C30 H20 N2 O10 . C8 H6 O4 . C2 H6 O2)x
CI PMS

CM 1



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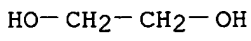

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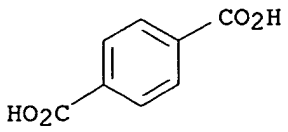
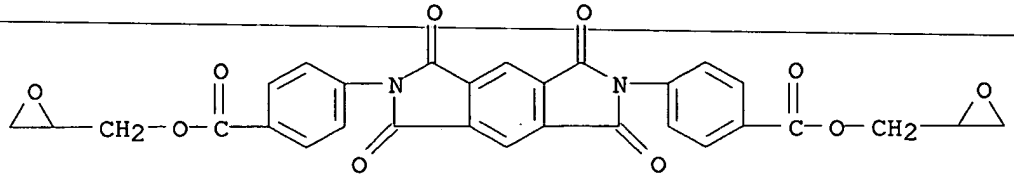
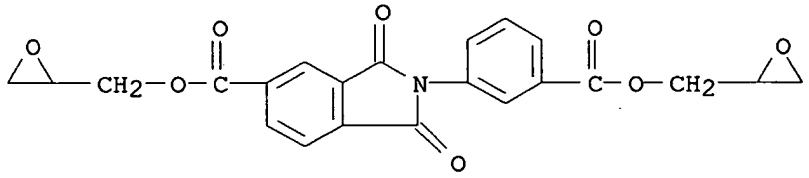


L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Benzoic acid, 4,4'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI)
MF C30 H20 N2 O10
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

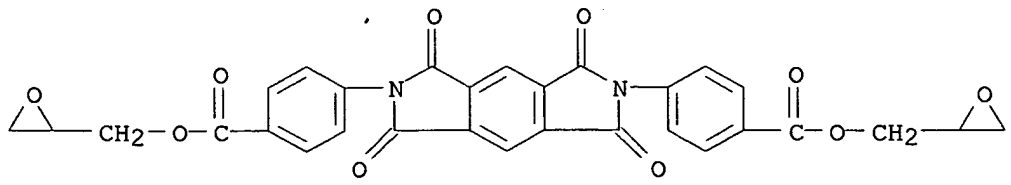
L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[3-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester (9CI)
MF C22 H17 N O8
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1,4-Benzenedicarboxylic acid, polymer with bis(oxiranylmethyl) 4,4'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis[benzoate] and 1,4-butanediol (9CI)
MF (C30 H20 N2 O10 . C8 H6 O4 . C4 H10 O2)x
CI PMS

CM 1



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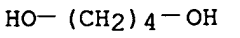

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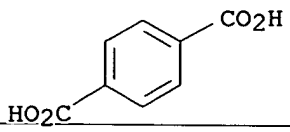
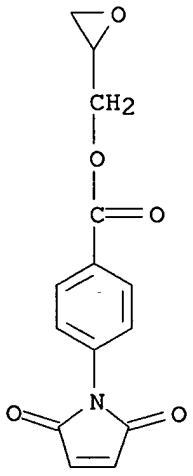
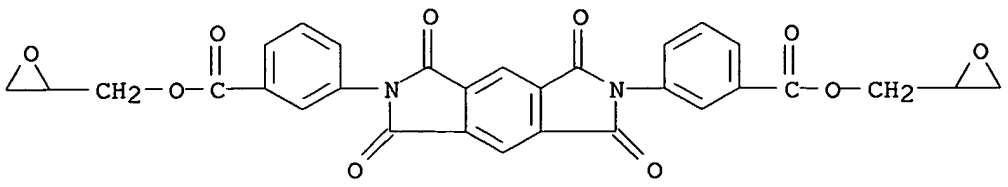


L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Benzoic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, oxiranylmethyl ester (9CI)
MF C14 H11 N O5



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

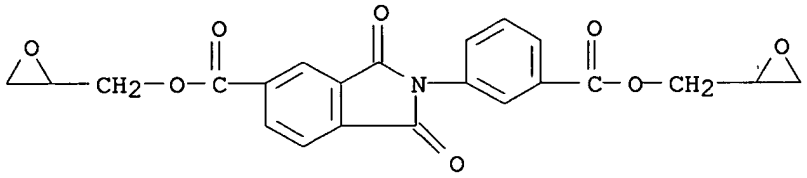
L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Benzoic acid, 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI)
MF C30 H20 N2 O10
CI COM



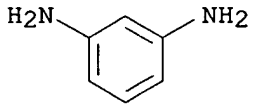
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[3-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester, polymer with 1,3-benzenediamine (9CI)
MF (C22 H17 N O8 . C6 H8 N2)x
CI PMS

CM 1

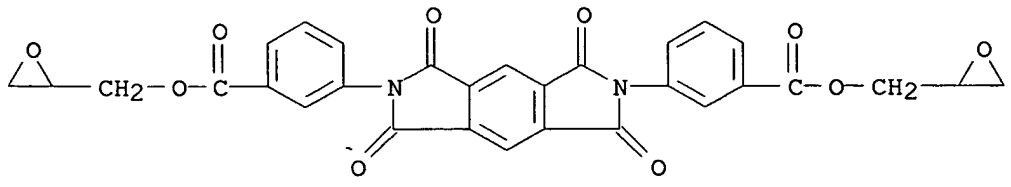


CM 2



L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN 1,4-Benzenedicarboxylic acid, polymer with bis(oxiranylmethyl) 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis[benzoate] and 1,4-butanediol (9CI)
MF (C30 H20 N2 O10 . C8 H6 O4 . C4 H10 O2)x
CI PMS

CM 1



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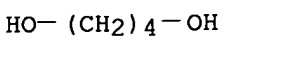
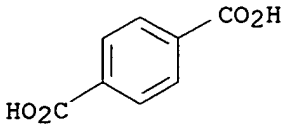
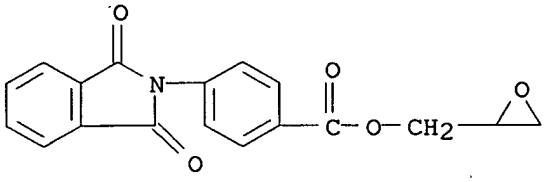


CM 3



L3 15 ANSWERS REGISTRY COPYRIGHT 2004 ACS on STN
IN Benzoic acid, 4-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-, oxiranylmethyl ester (9CI)
MF C18 H13 N O5



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ALL ANSWERS HAVE BEEN SCANNED

=> fil caold caplus; s L3

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FULL ESTIMATED COST	156.26	156.47

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L4 13 L3

=> d ibib abs hitstr L4 1-13

L4 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:608780 CAPLUS
DOCUMENT NUMBER: 141:278266
TITLE: Identification of rheological and structural characteristics of foamable poly(ethylene terephthalate) by reactive extrusion
AUTHOR(S): Xanthos, M.; Wan, C.; Dhavalikar, R.; Karayannidis, G.

P.; Bikiaris, D. N.

CORPORATE SOURCE: Polymer Processing Institute, New Jersey Institute of Technology, Newark, NJ, 07102, USA

SOURCE: Polymer International (2004), 53(8), 1161-1168
CODEN: PLYIEI; ISSN: 0959-8103

PUBLISHER: John Wiley & Sons Ltd.

DOCUMENT TYPE: Journal

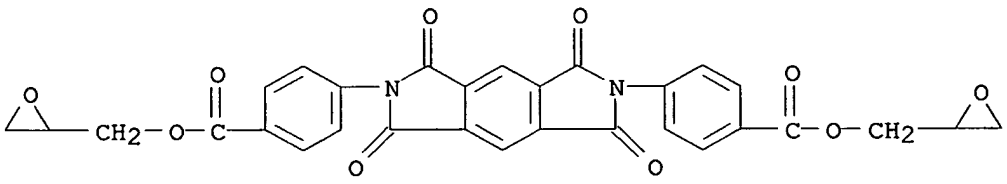
LANGUAGE: English

AB The reactivity and efficiency of five low-mol.-weight multifunctional anhydride and epoxy compds. as chemical modifiers of a bottle grade poly(ethylene terephthalate) (PET) resin were evaluated by reactive extrusion under controlled conditions. The two dianhydrides and the three epoxy compds. were used at concns. based on stoichiometry derived from the measured carboxyl and hydroxyl end group contents of the base resin. Measures of melt viscosity, melt strength, intrinsic viscosity and carboxyl group content were used as criteria of the extent of the modification. Correlations of die pressure with extrudate swell during extrusion, and melt flow index (MFI) with melt strength by off-line testing of the extrudates permitted the ranking of the modifiers according to their chain-extending/branching efficiency. For some systems mol. weight increases (related to die pressure/MFI/intrinsic viscosity) accompanied by broadening of the mol. weight distribution (related to die swell/melt strength) were considered excessive. Extrusion foaming expts. with one particular dianhydride modifier that increased the intrinsic viscosity of the resin from 0.71 to 0.9 dL g-1 indicate that production of low-d. foams by a process involving one-step reactive modification/gas injection foaming is feasible, at conditions not significantly different from those employed in the simple reactive modification of the PET resin. The rheol. and structural parameters determined in this work may be used as criteria to specify PET foamable compns. in terms of types and concns. of modifiers.

IT **97663-60-0DP**, reaction products with poly(ethylene terephthalate)
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(identification of rheol. and structural characteristics of foamable poly(ethylene terephthalate) modified with anhydride and epoxy compds. by reactive extrusion)

RN 97663-60-0 CAPLUS

CN Benzoic acid, 4,4'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:919736 CAPLUS

DOCUMENT NUMBER: 138:154316

TITLE: Parameters affecting the chain extension and branching of PET in the melt state by polyepoxides

AUTHOR(S): Dhavalikar, R.; Xanthos, M.

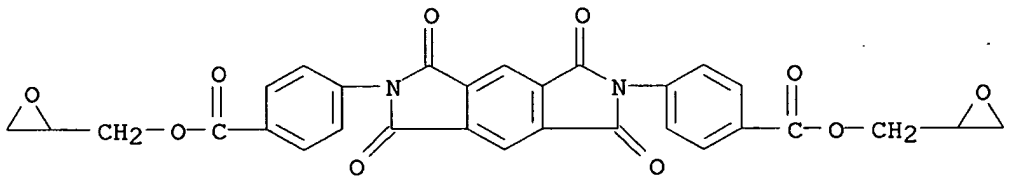
CORPORATE SOURCE: Department of Chemical Engineering, New Jersey Institute of Technology, Newark, NJ, 07102-1982, USA

SOURCE: Journal of Applied Polymer Science (2003), 87(4),

643-652
CODEN: JAPNAB; ISSN: 0021-8995
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This article describes the chemical modification of polyethylene terephthalate (PET) with a variety of compds. containing reactive glycidyl group(s). Four different modifiers, namely, diglycidyl ether of bisphenol-A (DGEBA), N,N'-bis[3(carbo-2',3'-epoxypropoxy) phenyl] pyromellitimide (BGPM), triglycidyl glycerol (TGG), and triglycidyl isocyanurate (TGIC) were compared for their reactivity toward PET in the melt phase. He presence of tertiary nitrogen in the structure of the epoxide modifiers plays the role of in-built catalyst for their reaction with the end groups of PET. TGIC as a modifier was selected for the detailed investigation of the simultaneously occurring degradation and chain extension/branching reactions in a batch-melt mixer. The reactions were followed by torque changes, analyzing the products for residual carboxyl content, and by determining insol. content. The rate of the reactive modification of PET melt by TGIC depends upon stoichiometry, temperature, rate of shear, and the chemical composition and the mol. weight (MW) of the PET resin. In general, the results indicate an increase in melt viscosity and insol. content, whereas an overall decrease in carboxyl content occurs, as defined by the choice of mixing conditions and stoichiometry. Anal. of the batch kinetic data can be useful to define the process requirements for carrying out the reactive modification in continuous extrusion equipment.

IT **97663-60-0**
RL: MOA (Modifier or additive use); USES (Uses)
(parameters affecting chain extension and branching of PET in melt state by epoxides)
RN 97663-60-0 CAPLUS
CN Benzoic acid, 4,4'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:572817 CAPLUS
DOCUMENT NUMBER: 138:107529
TITLE: Comparison of PET chemical modifiers for extrusion foaming
AUTHOR(S): Xanthos, M.; Dhavalikar, R.; Wan, C.; Zhang, Q.; Dey, S. K.
CORPORATE SOURCE: Polymer Processing Institute, Multilife-Cycle Engineering Research Center, New Jersey Institute of Technology, Newark, NJ, 07102, USA
SOURCE: Annual Technical Conference - Society of Plastics Engineers (2002), 60th(Vol. 2), 1876-1880
CODEN: ACPED4; ISSN: 0272-5223
PUBLISHER: Society of Plastics Engineers
DOCUMENT TYPE: Journal

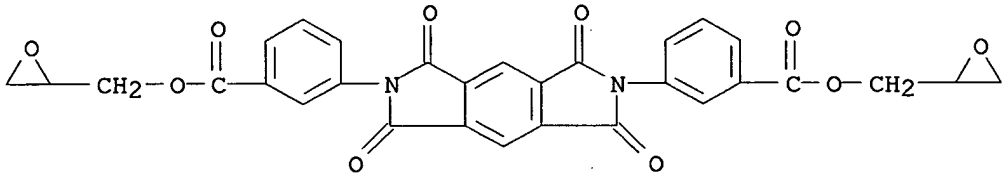
LANGUAGE: English

AB The efficiency of low mol. weight multifunctional anhydride and epoxy compds. as chemical modifiers for low d. extrusion foaming of low intrinsic viscosity (IV) polyethylene terephthalate (PET) was evaluated by reactive extrusion under controlled conditions. The two dianhydrides and the three epoxy compds. with different functionalities were used at concns. based on stoichiometry derived from the measured carboxyl and hydroxyl end group contents of the base resin. Correlations of die pressure with extrudate swell during extrusion, and melt flow index with melt strength by off-line testing of the extrudates permitted the ranking of the modifiers according to their chain-extending efficiency. Extrusion foaming expts. indicate that production of low-d. foams by a process involving one-step reactive modification/gas injection foaming is feasible, at conditions not significantly different than those employed in the simple reactive modification of the PET resin.

IT **97663-61-1**
RL: MOA (Modifier or additive use); USES (Uses)
(modifier; comparison of PET chemical modifiers for extrusion foaming)

RN 97663-61-1 CAPLUS

CN Benzoic acid, 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:562262 CAPLUS
DOCUMENT NUMBER: 136:200799
TITLE: Melt modification of PET with reactive glycidyl compounds
AUTHOR(S): Dhavalikar, R.; Xanthos, M.
CORPORATE SOURCE: Department of Chemical Engineering, Chemistry and Environmental Science, New Jersey Institute of Technology, Newark, NJ, 07102, USA
SOURCE: Annual Technical Conference - Society of Plastics Engineers (2001), 59th(Vol. 3), 2677-2682
CODEN: ACPED4; ISSN: 0272-5223
PUBLISHER: Society of Plastics Engineers
DOCUMENT TYPE: Journal
LANGUAGE: English

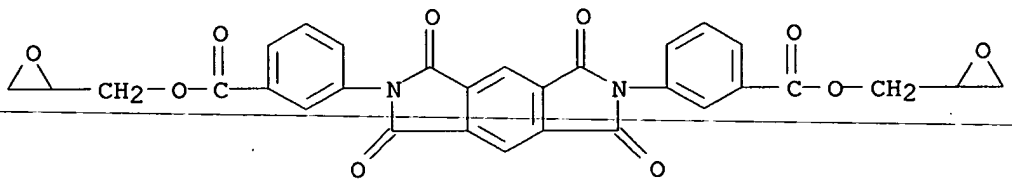
AB Melt strength of polyesters for foam extrusion and extrusion blow molding is controlled by weight-average mol. weight, mol. weight distribution, and the degree of branching. This paper describes the chemical modification of poly(ethylene terephthalate) (PET) as a technique to improve its melt strength using compds. containing the reactive glycidyl (epoxy) group. Preliminary evaluation of reactivity of multifunctional epoxides with poly(ethylene terephthalate) (PET) during melt mixing and selection of the most suitable epoxide and its concentration for modification of PET in extrusion foaming were carried out. The effect of addition of di-, tri-, and tetra-functional epoxy compds. to the PET resin in the melt state was studied using a batch mixer. Changes in the torque and temperature in the mixer

resulting from the addition of modifier(s) were followed in order to relate to the kinetics of the reactions.

IT **97663-61-1DP**, reaction products with poly(ethylene terephthalate)
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(melt modification of poly(ethylene terephthalate) with reactive glycidyl compds.)

RN 97663-61-1 CAPLUS

CN Benzoic acid, 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:296125 CAPLUS

DOCUMENT NUMBER: 135:77613

TITLE: Reactive modification of polyethylene terephthalate with polyepoxides

AUTHOR(S): Xanthos, M.; Young, M-W.; Karayannidis, G. P.; Bikiaris, D. N.

CORPORATE SOURCE: Polymer Processing Institute, N.J. Institute of Technology, Newark, NJ, 07102, USA

SOURCE: Polymer Engineering and Science (2001), 41(4), 643-655
CODEN: PYESAZ; ISSN: 0032-3888

PUBLISHER: Society of Plastics Engineers

DOCUMENT TYPE: Journal

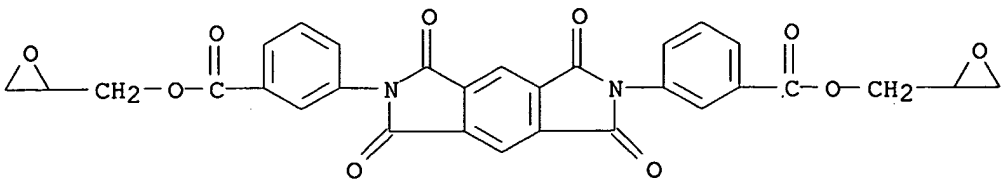
LANGUAGE: English

AB To produce modified PET resins with improved rheol. for applications requiring high viscosity and elasticity (e.g., low d. extrusion foaming, extrusion blow molding), N,N'-bis[3-[(glycidyloxy)carbonyl]phenyl]pyromellitimide was evaluated as a chain extender/branching agent. Its reactivity compares with that of ethylene/glycidyl methacrylate copolymer, and it can be used at much lower concns. The complex chain extension/degradation reactions occurring in the melt were followed in a batch mixer by torque changes, and by analyzing the products for residual carboxy and hydroxy content, intrinsic viscosity, insol. content and melt viscoelastic properties. The preliminary results indicate an overall decrease in carboxy content, an increase in hydroxy content, increased intrinsic viscosity and melt viscosity and storage modulus values depending on mixing time and the type and concentration of the additive. Under certain conditions, reaction of PET with <1 wt% diepoxide produces materials with rheol. characteristics similar to those of PET grades that are extrusion foamable by gas injection to low densities.

IT **97663-61-1**, N,N'-Bis[3-[(glycidyloxy)carbonyl]phenyl]pyromellitimide
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
(reactive modification of PET using bis[[(glycidyloxy)carbonyl]phenyl]pyromellitimide as chain extender)

RN 97663-61-1 CAPLUS

CN Benzoic acid, 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI) (CA INDEX NAME)



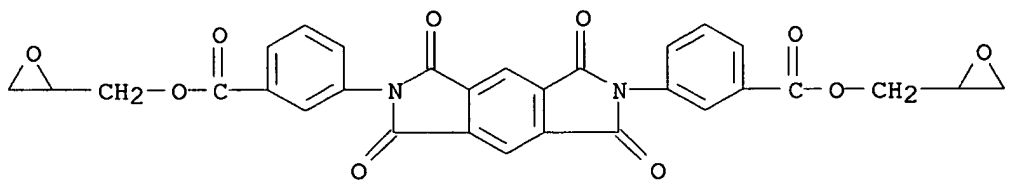
REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:81842 CAPLUS
DOCUMENT NUMBER: 132:208632
TITLE: Viscoelastic characteristics of chain extended/branched and linear polyethylene terephthalate resins
AUTHOR(S): Yilmazer, U.; Xanthos, M.; Bayram, G.; Tan, V.
CORPORATE SOURCE: Department of Chemical Engineering, Middle East Technical University, Ankara, Turk.
SOURCE: Journal of Applied Polymer Science (2000), 75(11), 1371-1377
CODEN: JAPNAB; ISSN: 0021-8995
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two chemical modified chain extended/branched polyethylene terephthalate (PET) resins and one unmodified resin, considered to be linear, were characterized in terms of their melt flow, die swell, and viscoelastic properties. The three resins had reportedly similar nominal intrinsic viscosities but exhibited different viscoelastic behavior. The modified resins had lower melt flow index, higher die swell, higher complex viscosity and higher storage modulus than the unmodified one. The Cole-Cole plots of the resins were independent of temperature, and the data for modified resins formed a group that lay below the data group for the unmodified PET. The distribution of relaxation times was determined The modified resins had higher relaxation strength, Gi, especially at high relaxation times, λi. The mean relaxation times of the chain extended/branched resins were approx. an order of magnitude higher than that of the unmodified resin, implying pronounced elastic character. The modified resins had better foaming characteristics in extrusion foam processing than the unmodified one owing to their elastic nature.

IT **97663-61-1**
RL: MOA (Modifier or additive use); USES (Uses)
(branching agent; viscoelasticity of branched and linear polyethylene terephthalate resins)

RN 97663-61-1 CAPLUS
CN Benzoic acid, 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI) (CA INDEX NAME)



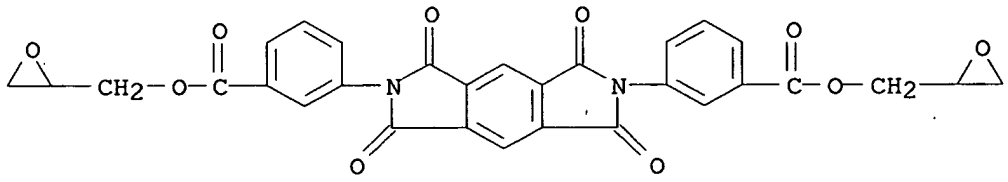
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:528631 CAPLUS
DOCUMENT NUMBER: 132:152447
TITLE: Rheological modification of PET by reactive processing with polyepoxides
AUTHOR(S): Young, M.-W.; Xanthos, M.; Karayannidis, G. P.; Bikiaris, D. N.
CORPORATE SOURCE: Polymer Processing Institute, Hoboken, NJ, 07030, USA
SOURCE: Annual Technical Conference - Society of Plastics Engineers (1999), 57th(Vol. 2), 2022-2026
CODEN: ACPED4; ISSN: 0272-5223
PUBLISHER: Society of Plastics Engineers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In attempts to produce modified PET resins with improved rheol. for applications requiring high viscosity and elasticity (e.g., foaming or extrusion blow molding), a novel low-mol.-weight diimidodiepoxide was evaluated as a chain extender/branching agent; its reactivity was compared with that of an ethylene-glycidyl methacrylate copolymer. Melt-modified products were characterized by end-group anal., intrinsic viscosity, and dynamic mech. properties. Under certain conditions, reaction with <1 weight% of the above diimidodiepoxide produced materials with rheol. characteristics similar to those of extrusion foamable by gas injection PET grades.

IT **97663-61-1**, Benzoic acid, 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester
RL: NUU (Other use, unclassified); RCT (Reactant); RACT (Reactant or reagent); USES (Uses)
(chain extender; reaction of PET with polyepoxide chain extenders for production of rheol. modified feedstocks for plastics processing)

RN 97663-61-1 CAPLUS
CN Benzoic acid, 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI) (CA INDEX NAME)

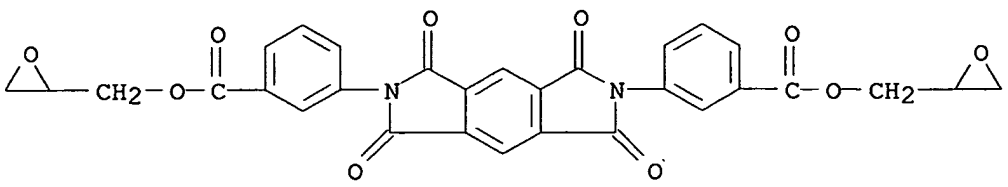


IT **164727-94-0P**
RL: PEP (Physical, engineering or chemical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(reaction of PET with polyepoxide chain extenders for production of rheol. modified feedstocks for plastics processing)

RN 164727-94-0 CAPLUS
CN 1,4-Benzenedicarboxylic acid, polymer with bis(oxiranylmethyl) 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis[benzoate] and 1,2-ethanediol (9CI) (CA INDEX NAME)

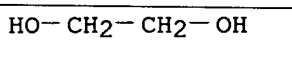
CM 1

CRN 97663-61-1
CMF C30 H20 N2 O10



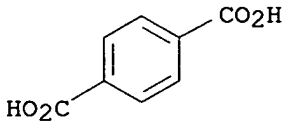
CM 2

CRN 107-21-1
CMF C2 H6 O2



CM 3

CRN 100-21-0
CMF C8 H6 O4



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:161673 CAPLUS
DOCUMENT NUMBER: 130:282614
TITLE: Effect of carboxylic end groups on thermooxidative stability of PET and PBT
AUTHOR(S): Bikiaris, Dimitris N.; Karayannidis, George P.
CORPORATE SOURCE: Laboratory of Organic Chemical Technology, Department of Chemistry, Aristotle University of Thessaloniki, Thessaloniki, Macedonia, GR-540 06, Greece
SOURCE: Polymer Degradation and Stability (1999), 63(2), 213-218
CODEN: PDSTDW; ISSN: 0141-3910
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of poly(ethylene terephthalate) and of poly(butylene terephthalate) samples containing different amts. of carboxyl end groups were prepared by chain-extension reaction with diepoxides. The effect of the carboxyl content on thermooxidative degradation was studied, using as criteria the induction period of oxidation and the stabilization coefficient, both obtained by differential scanning calorimetry during isothermal or dynamic heating of the samples under air and nitrogen atmospheric It was found that as the carboxyl content decreases the thermooxidative stability increases. However, in some more chain extended (crosslinked) samples the thermooxidative stability degreased. This abnormal behavior was attributed to the lower degree of crystallinity of these samples.

IT **164727-91-7**

RL: PRP (Properties)
(effect of carboxylic end groups on thermooxidative stability of PET and PBT)

RN 164727-91-7 CAPLUS

CN 1,4-Benzenedicarboxylic acid, polymer with bis(oxiranylmethyl) 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis[benzoate] and 1,4-butanediol (9CI) (CA INDEX NAME)

CM 1

CRN 97663-61-1
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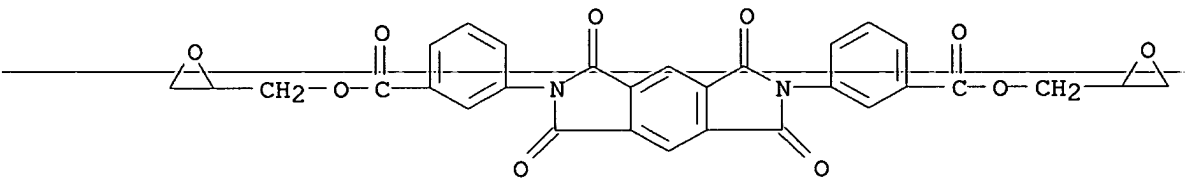
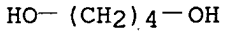


Tetrahedron 41(4) 767-76F (Dec 1985)

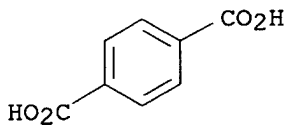
CM 2

CRN 110-63-4
CMF C4 H10 O2



CM 3

CRN 100-21-0
CMF C8 H6 O4



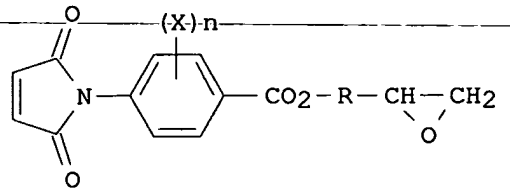
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:398245 CAPLUS
DOCUMENT NUMBER: 129:81659
TITLE: Epoxy group-containing esters of maleimidobenzoic acid or its derivatives
INVENTOR(S): Garapon, Jacques; Vallet, Jacques
PATENT ASSIGNEE(S): Institut Francais du Petrole, Fr.
SOURCE: Eur. Pat. Appl., 7 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

EP 848002	A1	19980617	EP 1997-402942	19971205
EP 848002	B1	20011010		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
FR 2757165	A1	19980619	FR 1996-15472	19961212
FR 2757165	B1	19990219		
ES 2165573	T3	20020316	ES 1997-402942	19971205
JP 10175973	A2	19980630	JP 1997-340916	19971211
US 5981763	A	19991109	US 1997-988683	19971211

PRIORITY APPLN. INFO.: FR 1996-15472 A 19961212
OTHER SOURCE(S): MARPAT 129:81659
GI



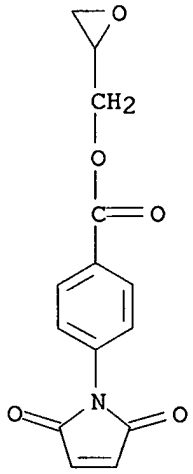
I

AB Title compds. I (R = divalent group, X = substituent, n = 0-4), useful for compatibilizers for polymer blends or functionalizing agents for polyolefins, are manufactured by esterification of the corresponding maleimidobenzoyl chloride with epoxy alcs.

IT **209266-05-7P**
RL: IMF (Industrial manufacture); PREP (Preparation)
(epoxy group-containing esters of maleimidobenzoic acid or its derivs.)

RN 209266-05-7 CAPLUS

CN Benzoic acid, 4-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-, oxiranylmethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:639686 CAPLUS
DOCUMENT NUMBER: 123:57317
TITLE: Chain extension of polyesters PET and PBT with

N,N'-bis(glycidyl ester) pyromellitimides. I

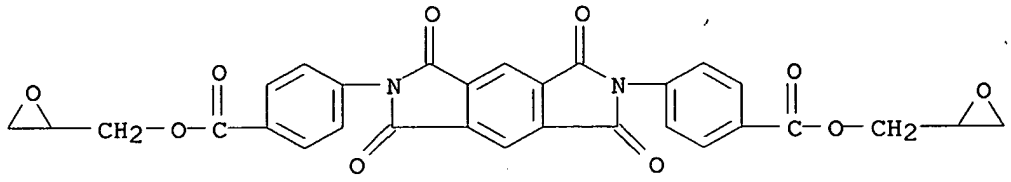
AUTHOR(S): Bikiaris, Demetris N.; Karayannidis, George P.
CORPORATE SOURCE: Dep. of Chemistry, Aristotle Univ. of Thessaloniki, Thessaloniki, GR-540 06, Greece

SOURCE: Journal of Polymer Science, Part A: Polymer Chemistry (1995), 33(10), 1705-14
CODEN: JPACEC; ISSN: 0887-624X
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

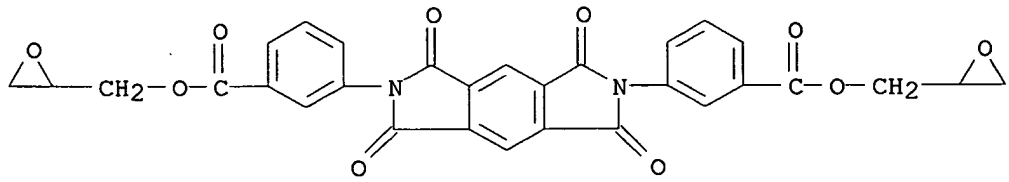
AB Three N,N'-bis(glycidyl ester imides) of pyromellitic acid were prepared and were used as chain extenders for poly(ethylene terephthalate) (PET) and poly(butylene terephthalate) (PBT). The typical reaction conditions for the coupling of the polyester macromols. were heating with the chain extender under argon atmospheric above the melting temperature (280° for PET and 250° for PBT) for several minutes. The characterization of the samples, obtained at variable residence times in the reactor, was based on solution viscosity measurements and carboxyl and hydroxyl end-group detns. Two of the diepoxides used gave satisfactory results. Starting from a PET having intrinsic viscosity [η] = 0.60 dL/g, and carboxyl content CC = 42 equiv/106 g, one could obtain PET with [η] = 1.15 dL/g and CC = 16 equiv/106 g within 30 min at 280°. Analogous results were observed for PBT. The hydroxyl content of polyester in all cases was increased. When the quantity of the chain extender used was higher than that theor. required for its reaction with all carboxyl end groups of the polyester, this resulted in some gel formation indicative of crosslinking.

IT **97663-60-0P 97663-61-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(chain extender; chain extension of polyesters using pyromellitimide bis(glycidyl) ester)

RN 97663-60-0 CAPLUS
CN Benzoic acid, 4,4'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI) (CA INDEX NAME)



RN 97663-61-1 CAPLUS
CN Benzoic acid, 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI) (CA INDEX NAME)



IT **164727-90-6P 164727-91-7P 164727-93-9P 164727-94-0P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)

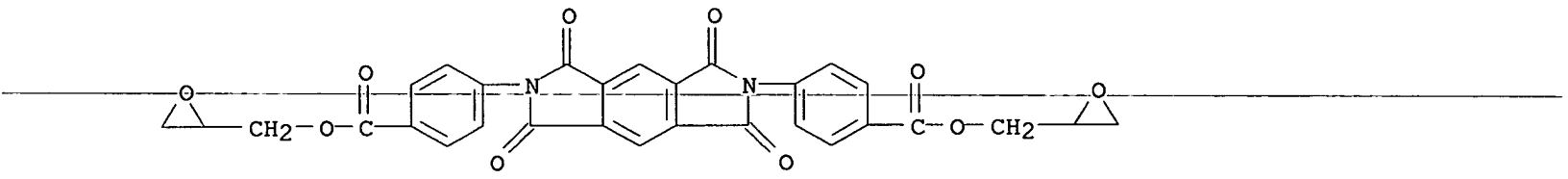
(chain extension of polyesters using pyromellitimide bis(glycidyl) ester)

RN 164727-90-6 CAPLUS

CN 1,4-Benzenedicarboxylic acid, polymer with bis(oxiranylmethyl) 4,4'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis[benzoate] and 1,4-butanediol (9CI) (CA INDEX NAME)

CM 1

CRN 97663-60-0
CMF C30 H20 N2 O10

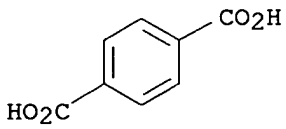


CM 2

CRN 110-63-4
CMF C4 H10 O2

CM 3

CRN 100-21-0
CMF C8 H6 O4

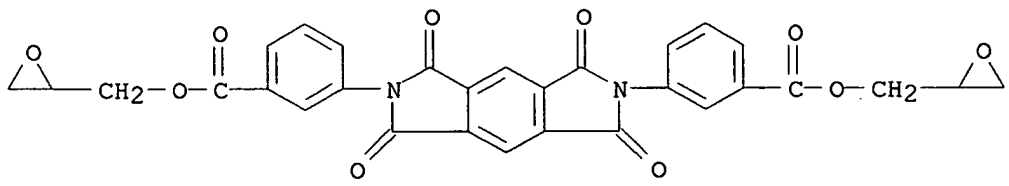


RN 164727-91-7 CAPLUS

CN 1,4-Benzenedicarboxylic acid, polymer with bis(oxiranylmethyl) 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis[benzoate] and 1,4-butanediol (9CI) (CA INDEX NAME)

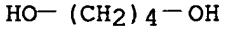
CM 1

CRN 97663-61-1
CMF C30 H20 N2 O10



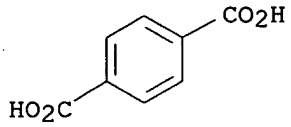
CM 2

CRN 110-63-4
CMF C4 H10 O2



CM 3

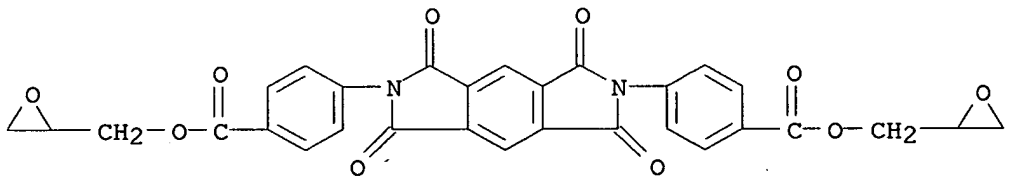
CRN 100-21-0
CMF C8 H6 O4



RN 164727-93-9 CAPLUS
CN 1,4-Benzenedicarboxylic acid, polymer with bis(oxiranylmethyl) 4,4'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis[benzoate] and 1,2-ethanediol (9CI) (CA INDEX NAME)

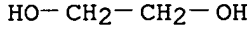
CM 1

CRN 97663-60-0
CMF C30 H20 N2 O10



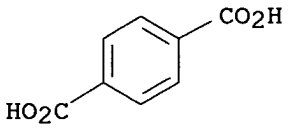
CM 2

CRN 107-21-1
CMF C2 H6 O2



CM 3

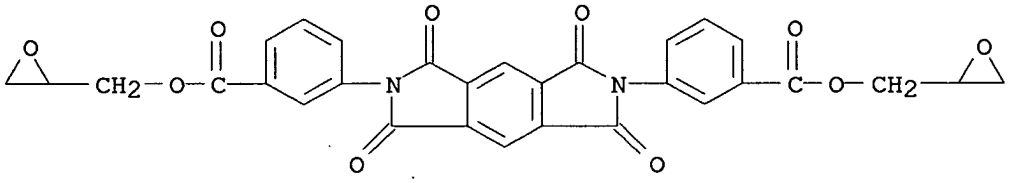
CRN 100-21-0
CMF C8 H6 O4



RN 164727-94-0 CAPLUS
CN 1,4-Benzenedicarboxylic acid, polymer with bis(oxiranylmethyl) 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis[benzoate] and 1,2-ethanediol (9CI) (CA INDEX NAME)

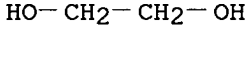
CM 1

CRN 97663-61-1
CMF C30 H20 N2 O10



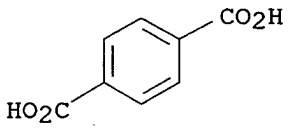
CM 2

CRN 107-21-1
CMF C2 H6 O2



CM 3

CRN 100-21-0
CMF C8 H6 O4

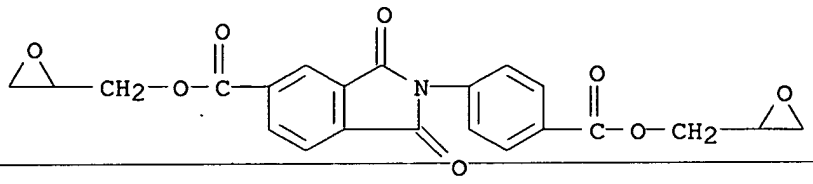


L4 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:151071 CAPLUS
DOCUMENT NUMBER: 108:151071
TITLE: Synthesis of asymmetric diglycidyl ester compounds - reaction with aromatic diamines
AUTHOR(S): Mantecon, Ana; Cadiz, Virginia; Serra, Angels; Martinez, Pedro Alberto
CORPORATE SOURCE: Fac. Quim., Univ. Barcelona, Tarragona, 43005, Spain
SOURCE: Angewandte Makromolekulare Chemie (1988), 156, 37-48
CODEN: ANMCBO; ISSN: 0003-3146
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Trimellitimide unit-containing diglycidyl esters were prepared and polymerized with

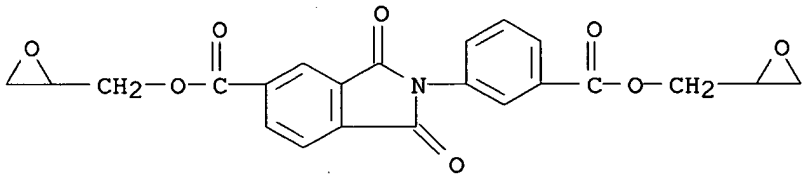
4,4'-diaminodiphenylmethane or m-phenylenediamine to give crosslinked resins. Thermal stability of the crosslinked resins was determined

IT **113602-06-5P 113602-08-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and copolymn. of)

RN 113602-06-5 CAPLUS
CN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[4-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester (9CI) (CA INDEX NAME)



RN 113602-08-7 CAPLUS
CN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[3-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester (9CI) (CA INDEX NAME)

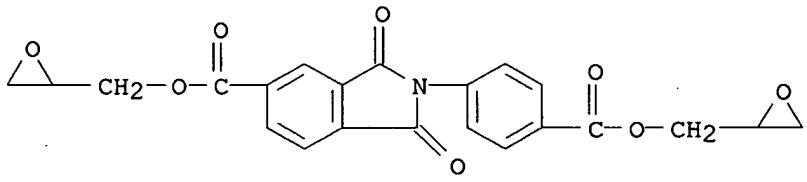


IT **113602-07-6P 113602-09-8P 113602-10-1P**
113602-11-2P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and thermal stability of)

RN 113602-07-6 CAPLUS
CN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[4-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester, polymer with 1,3-benzenediamine (9CI) (CA INDEX NAME)

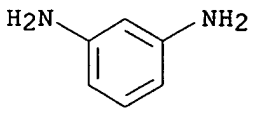
CM 1

CRN 113602-06-5
CMF C22 H17 N O8



CM 2

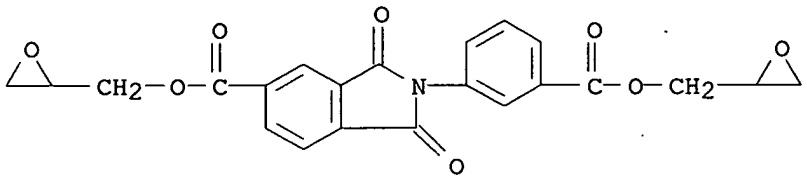
CRN 108-45-2
CMF C6 H8 N2



RN 113602-09-8 CAPLUS
CN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[3-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester, polymer with 1,3-benzenediamine (9CI) (CA INDEX NAME)

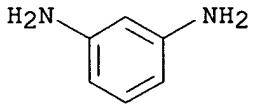
CM 1

CRN 113602-08-7
CMF C22 H17 N O8



CM 2

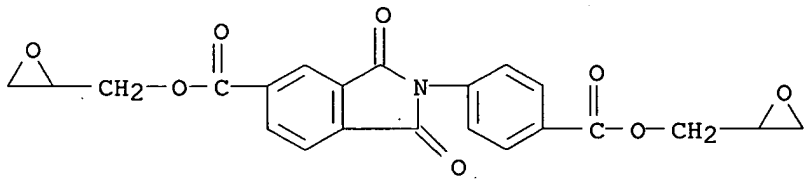
CRN 108-45-2
CMF C6 H8 N2



RN 113602-10-1 CAPLUS
CN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[4-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester, polymer with 4,4'-methylenebis[benzenamine] (9CI) (CA INDEX NAME)

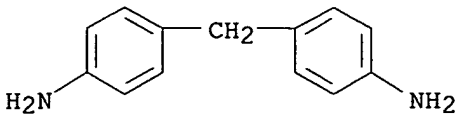
CM 1

CRN 113602-06-5
CMF C22 H17 N O8



CM 2

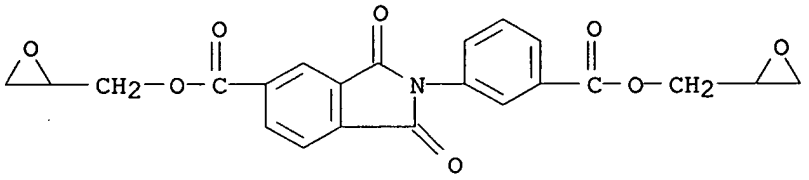
CRN 101-77-9
CMF C13 H14 N2



RN 113602-11-2 CAPLUS
CN 1H-Isoindole-5-carboxylic acid, 2,3-dihydro-2-[3-[(oxiranylmethoxy)carbonyl]phenyl]-1,3-dioxo-, oxiranylmethyl ester, polymer with 4,4'-methylenebis[benzenamine] (9CI) (CA INDEX NAME)

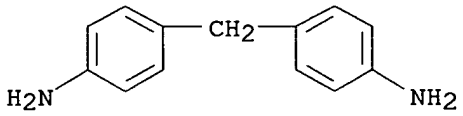
CM 1

CRN 113602-08-7
CMF C22 H17 N O8



CM 2

CRN 101-77-9
CMF C13 H14 N2



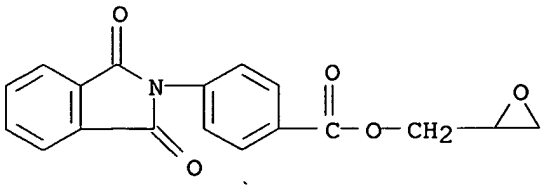
L4 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:554797 CAPLUS
DOCUMENT NUMBER: 107:154797
TITLE: Oxirane ring opening with imide acids
AUTHOR(S): Soler, Hector; Cadiz, Virginia; Serra, Angels
CORPORATE SOURCE: Fac. Quim. Tarragona, Univ. Barcelona, Tarragona, Spain
SOURCE: Angewandte Makromolekulare Chemie (1987), 152, 55-60
CODEN: ANMCBO; ISSN: 0003-3146
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A study with model compds. was made by 13C-NMR in order to confirm the 2 possible sites of attack on an oxirane ring by a carboxylic acid. In all cases the presence of signals corresponding to normal and abnormal opening of the ring was detected. Thus, 2 different methods to quantify the obtained primary and secondary alc. amts. were used. The less primary alc. was obtained the more nucleophilic the carboxylic acid was.

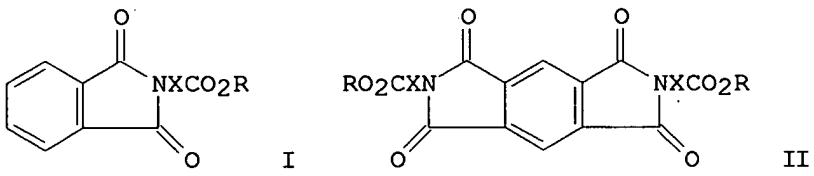
IT **97663-55-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with imide acids, as model for epoxy-polyester-polyimide formation)

RN 97663-55-3 CAPLUS
CN Benzoic acid, 4-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-, oxiranylmethyl

ester (9CI) (CA INDEX NAME)



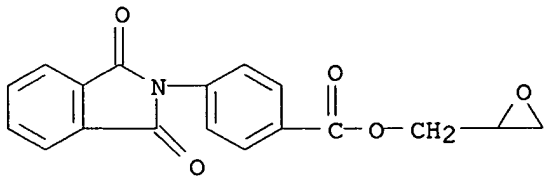
L4 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1985:471152 CAPLUS
DOCUMENT NUMBER: 103:71152
TITLE: New glycidyl ester compounds containing a preformed imide ring - I
AUTHOR(S): Serra, A.; Cadiz, V.; Mantecon, A.; Martinez, P. A.
CORPORATE SOURCE: Fac. Quim., Univ. Barcelona, Tarragona, Spain
SOURCE: Tetrahedron (1985), 41(4), 763-8
CODEN: TETRAB; ISSN: 0040-4020
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 103:71152
GI



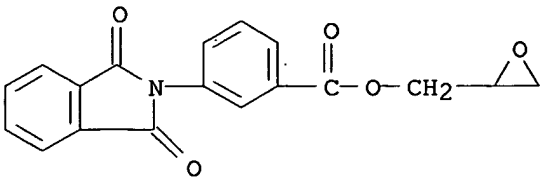
AB Glycidyl esters I and II [R = glycidyl; X = CH2, (CH2)3, (CH2)5, 1,3-phenylene, 1,4-phenylene] were prepared by condensation of I and II (R = H) with a large excess of epichlorohydrin. The structure of glycidyl esters was determined by elementary anal., IR and 1H and 13C NMR spectra. The phys. properties were also defined.

IT **97663-55-3P 97663-56-4P 97663-60-0P 97663-61-1P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and NMR of)

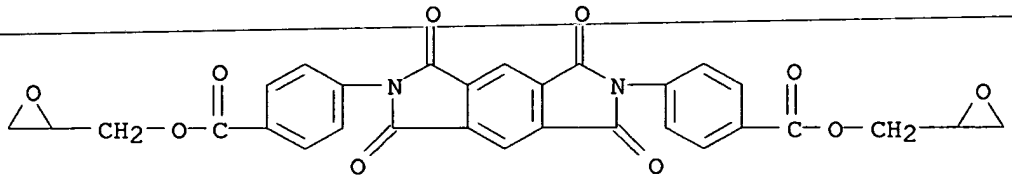
RN 97663-55-3 CAPLUS
CN Benzoic acid, 4-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-, oxiranylmethyl ester (9CI) (CA INDEX NAME)



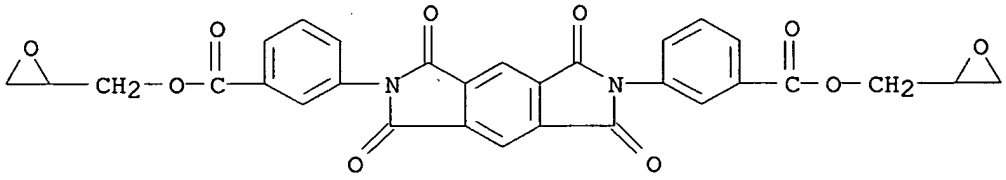
RN 97663-56-4 CAPLUS
CN Benzoic acid, 3-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)-, oxiranylmethyl ester (9CI) (CA INDEX NAME)



RN 97663-60-0 CAPLUS
CN Benzoic acid, 4,4'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI) (CA INDEX NAME)



RN 97663-61-1 CAPLUS
CN Benzoic acid, 3,3'-(5,7-dihydro-1,3,5,7-tetraoxobenzo[1,2-c:4,5-c']dipyrrole-2,6(1H,3H)-diyl)bis-, bis(oxiranylmethyl) ester (9CI) (CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 11:11:18 ON 19 NOV 2004)

FILE 'REGISTRY' ENTERED AT 11:11:29 ON 19 NOV 2004
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 15 S L1 FULL

FILE 'CAOLD, CAPLUS' ENTERED AT 11:13:33 ON 19 NOV 2004
L4 13 S L3

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	64.06	220.53
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.10	-9.10

STN INTERNATIONAL LOGOFF AT 11:15:54 ON 19 NOV 2004